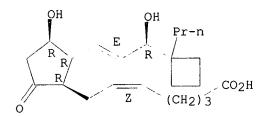
RN 63357-25-5 HCAPLUS

CN 5-Heptenoic acid, 7-[3-hydroxy-2-[3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxocyclopentyl]-, [1.alpha.(Z), 2.beta.(1E, 3R\*), 3.alpha.]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

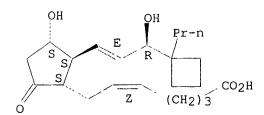
Double bond geometry as shown.



RN 63357-26-6 HCAPLUS

CN 5-Heptenoic acid, 7-[3-hydroxy-2-[3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.]-(9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.



L115 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

AN 1/977:463008 HCAPLUS

DN 87:63008

TI Prostaglandins and congeners. 14. Synthesis and bronchodilator activity of dl-16,16-trimethyleneprostaglandins

AU Skotnicki, Jerauld S.; Schaub, Robert E.; Weiss, Martin J.; Dessy, F.

CS Lederle Lab., Am. Cyanamid Co., Pearl River, N. Y., USA

SO J. Med. Chem. (1977), 20(8), 1042-7 CODEN: JMCMAR

DT Journal

LA English

CC 2-3 (Hormone Pharmacology)
Section cross-reference(s): 24

GΙ

```
OH I, R=(CH<sub>2</sub>)<sub>6</sub>CO<sub>2</sub>H
II, R=z-CH=CH(CH<sub>2</sub>)<sub>3</sub>CO<sub>2</sub>H
```

```
AΒ
    A series of 33 title compds. was prepd. by the lithiocuprate conjugate
     addn. of a fully elaborated .beta. chain to the several cyclopentenones
    with varying .alpha. chains. The bronchodilator effect of the compds. was
     detd. by i.v. administration to guinea pigs previously treated with
     serotonin, histamine, or acetylcholine. The most active compds.,
    dl-16,16-trimethyleneprostaglandin E1 (I) [63357-23-3] and
    dl-16,16-trimethyleneprostaglandin E2 (II) [62446-43-9
     , gave results comparable to 1-prostaglandin El. Structure-activity
    relations are discussed.
ST
    bronchodilator prostaglandin cyclic trimethylene analog;
     trimethyleneprostaglandin analog bronchodilator
ΙT
    Bronchodilators
        (prostaglandin cyclic trimethylene analogs)
IT
    Molecular structure-biological activity relationship
        (bronchodilating, of prostaglandin cyclic trimethylene
        analogs)
IT
     Prostaglandins
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (cyclic trimethylene analogs, prepn. and bronchodilator
        activity of)
                  50999-85-4
ΙT
     41264-03-3
    RL: RCT (Reactant)
        (alkylation of)
TΥ
     40899-59-0
    RL: RCT (Reactant)
        (oxidn. of)
IT
     40098-44-0P
                   63295-68-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and alkylation of)
IT
     363-24-6DP, cyclic trimethylene analog
                                              745-65-3DP, cyclic
                                         62446-40-6P
     trimethylene analog
                           62407-92-5P
                                                        62446-41-7P
     62446-42-8P 62446-43-9P
                               63295-70-5P
                                             63295-71-6P
     63295-72-7P
                   63295-73-8P
                                 63295-74-9P
                                                63295-75-0P
                                                              63295-76-1P
                                                              63295-81-8P
     63295-77-2P
                   63295-78-3P
                                 63295-79-4P
                                                63295-80-7P
     63357-23-3P
                   63357-24-4P 63357-25-5P 63357-26-6P
     63357-27-7P
                   63357-28-8P
                                 63357-29-9P
                                                63357-30-2P
                                                              63357-31-3P
     63357-32-4P
                   63357-33-5P
                                 63357-34-6P
                                                63357-35-7P
                                                              63357-36-8P
    63492-48-8P
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and bronchodilator activity of)
     63295-67-0P
IT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and cyclopentenone deriv. alkylation by)
     40899-63-6P
IT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and esterification of)
     63295-69-2P
ΙT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and hydrolysis of)
ΙT
     63295-66-9P
```

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

RN 63357-25-5 HCAPLUS

CN 5-Heptenoic acid, 7-[3-hydroxy-2-[3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.]-(9CI) (CA INDEX NAME)

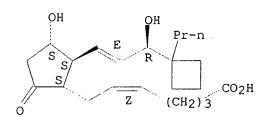
Relative stereochemistry.

Double bond geometry as shown.

RN 63357-26-6 HCAPLUS

CN 5-Heptenoic acid, 7-[3-hydroxy-2-[3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.]-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L115 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

1977:463008 HCAPLUS

DN 87:63008

TI Prostaglandins and congeners. 14. Synthesis and bronchodilator activity of dl-16,16-trimethyleneprostaglandins

1,50

- AU Skotnicki, Jerauld S.; Schaub, Robert E.; Weiss, Martin J.; Dessy, F.
- CS Lederle Lab., Am. Cyanamid Co., Pearl River, N. Y., USA
- SO J. Med. Chem. (1977), 20(8), 1042-7

CODEN: JMCMAR

- DT Journal
- LA English
- CC 2-3 (Hormone Pharmacology)
   Section cross-reference(s): 24

GI

```
OH II, R=(CH<sub>2</sub>)<sub>6</sub>CO<sub>2</sub>H II, R=z-CH=CH(CH<sub>2</sub>)<sub>3</sub>CO<sub>2</sub>H
```

```
AB
     A series of 33 title compds. was prepd. by the lithiocuprate conjugate
     addn. of a fully elaborated .beta. chain to the several cyclopentenones
     with varying .alpha. chains. The bronchodilator effect of the compds. was
     detd. by i.v. administration to guinea pigs previously treated with
     serotonin, histamine, or acetylcholine. The most active compds.,
     dl-16,16-trimethyleneprostaglandin E1 (I) [63357-23-3] and
     dl-16,16-trimethyleneprostaglandin E2 (II) [62446-43-9
     ], gave results comparable to 1-prostaglandin E1. Structure-activity
     relations are discussed.
     bronchodilator prostaglandin cyclic trimethylene analog;
ST
     trimethyleneprostaglandin analog bronchodilator
IT
     Bronchodilators
         (prostaglandin cyclic trimethylene analogs)
     Molecular structure-biological activity relationship
IT
        (bronchodilating, of prostaglandin cyclic trimethylene
        analogs)
ΙT
     Prostaglandins
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (cyclic trimethylene analogs, prepn. and bronchodilator
        activity of)
IT
     41264-03-3
                   50999-85-4
     RL: RCT (Reactant)
        (alkylation of)
ΙT
     40899-59-0
     RL: RCT (Reactant)
        (oxidn. of)
IT
     40098-44-0P
                   63295-68-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and alkylation of)
IT
     363-24-6DP, cyclic trimethylene analog
                                               745-65-3DP, cyclic
                            62407-92-5P
     trimethylene analog
                                          62446-40-6P
                                                        62446-41-7P
     62446-42-8P 62446-43-9P
                                63295-70-5P
                                              63295-71-6P
     63295-72-7P
                   63295-73-8P
                                  63295-74-9P
                                                63295-75-0P
                                                              63295-76-1P
     63295-77-2P
                   63295-78-3P
                                  63295-79-4P
                                                63295-80-7P
                                                              63295-81-8P
     63357-23-3P
                   63357-24-4P 63357-25-5P 63357-26-6P
     63357-27-7P
                   63357-28-8P
                                  63357-29-9P
                                                63357-30-2P
                                                              63357-31-3P
     63357-32-4P
                   63357-33-5P
                                  63357-34-6P
                                                63357-35-7P
                                                              63357-36-8P
     63492-48-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and bronchodilator activity of)
IT
     63295-67-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and cyclopentenone deriv. alkylation by)
IT
     40899-63-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and esterification of)
IT
     63295-69-2P
```

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and hydrolysis of)

IT

63295-66-9P

#### => d ide can tot

L171 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2002 ACS

RN 19313-28-1 REGISTRY

CN Prostan-1-oic acid, 11,15-dihydroxy-9-oxo-, (11.alpha.,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 3-hydroxy-2-(3-hydroxyoctyl)-5-oxo-, stereoisomer (8CI)

### OTHER NAMES:

CN (15S) - Dihydroprostaglandin El

CN 11,15-Dihydroxy-9-ketoprostanoic acid

CN 11.alpha.,15-Dihydroxy-9-oxoprostanoic acid

CN 13,14-Dihydro-PGE1

CN 13,14-Dihydroprostaglandin El

CN Dihydro-PGE1

CN Dihydroprostaglandin E1

CN PGE0

CN prostaglandin E0

CN U 23307

FS STEREOSEARCH

DR 23923-86-6, 19338-39-7, 23452-94-0, 23621-67-2, 5094-13-3, 28527-86-8

MF C20 H36 O5

CI COM

LC STN Files: BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CHEMCATS, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)

#### Absolute stereochemistry.

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

97 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

97 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:333176

REFERENCE 2: 137:88720

REFERENCE 3: 136:145563

REFERENCE 4: 136:694

REFERENCE 5: 135:231699

REFERENCE 6: 135:190765

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

REFERENCE 7: 135:147536

REFERENCE 8: 135:56407

REFERENCE 9: 135:29385

REFERENCE 10: 133:271683

L171 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2002 ACS

RN 10164-73-5 REGISTRY

CN Prost-13-en-1-oic acid, 9,11,15-trihydroxy-, (9.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 3,5-dihydroxy-2-(3-hydroxy-1-octenyl)-, stereoisomer (8CI)

OTHER NAMES:

CN PGF1.beta.

CN Prostaglandin F1.beta.

FS STEREOSEARCH

DR 21562-48-1, 28977-21-1

MF C20 H36 O5

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, TOXCENTER, USPATFULL (\*File contains numerically searchable property data)

Absolute stereochemistry.

Double bond geometry as shown.

# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

64 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

¥

64 REFERENCES IN FILE CAPLUS (1962 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 128:132260

REFERENCE 2: 115:223767

REFERENCE 3: 109:92548

REFERENCE 4: 101:222865

REFERENCE 5: 101:129876

REFERENCE 6: 97:72140

REFERENCE 7: 96:15330

REFERENCE 8: 96:976

1

REFERENCE 9: 96:975

REFERENCE 10: 95:164870

L171 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2002 ACS

RN 4510-16-1 REGISTRY

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,

(5Z, 9.beta., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-, stereoisomer (8CI)

OTHER NAMES:

CN 7-[3.alpha.,5.beta.-Dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-5heptenoic acid

CN 9.beta.,11.alpha.-PGF2.alpha.

CN PGF2.beta.

CN Prostaglandin F2.beta.

FS STEREOSEARCH

DR 89847-01-8

MF C20 H34 O5

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, MEDLINE, RTECS\*, TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)

Absolute stereochemistry.

Double bond geometry as shown.

HO

R

R

R

E

S

$$(CH_2)_4$$

Me

HO

OH

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

163 REFERENCES IN FILE CA (1962 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

164 REFERENCES IN FILE CAPLUS (1962 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:147536

REFERENCE 2: 135:730

REFERENCE 3: 134:361713

REFERENCE 4: 133:161954

REFERENCE 5: 133:924

REFERENCE 6: 131:295642

REFERENCE 7: 131:252650

REFERENCE 8: 130:320932

REFERENCE 9: 130:205253

REFERENCE 10: 130:119579

L171 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2002 ACS

RN 802-31-3 REGISTRY

CN Prosta-5,13,17-trien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11.alpha.,13E,15S,17Z)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3-hydroxy-2-(3-hydroxy-1,5-octadienyl)-5-oxocyclopentyl]-, stereoisomer (8CI)

OTHER NAMES:

CN (-)-Prostaglandin E3

CN PGE3

CN Prostaglandin E3

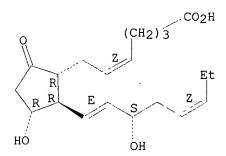
FS STEREOSEARCH

MF C20 H30 O5

CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, TOXCENTER, USPATFULL (\*File contains numerically searchable property data)

Absolute stereochemistry. Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*.

155 REFERENCES IN FILE CA (1962 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

155 REFERENCES IN FILE CAPLUS (1962 TO DATE)

11 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:333176

REFERENCE 2: 137:307621

REFERENCE 3: 137:246360

REFERENCE 4: 137:195936

REFERENCE 5: 136:406871

REFERENCE 6: 136:145563

7

```
REFERENCE
            7:
                136:64154
REFERENCE
            8:
                136:17461
                135:231699
REFERENCE
            9:
REFERENCE 10: 135:147536
L171 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2002 ACS
     745-65-3 REGISTRY
RN
     Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-, (11.alpha.,13E,15S)- (9CI)
CN
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Cyclopentaneheptanoic acid, 3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxo-, (-)-
CN
     Cyclopentaneheptanoic acid, 3.alpha.-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxo-
      (7CI)
OTHER NAMES:
     (-)-Prostaglandin El
CN
     11.alpha., 15(S)-Dihydroxy-9-oxo-13-trans-prostenoic acid
CN
CN
     11.alpha., 15.alpha.-Dihydroxy-9-oxo-13-trans-prostenoic acid
CN
     Alprostadil
CN
     Alprox TD
CN
     Caverject
CN
     1-PGE1
CN
     1-Prostaglandin E1
CN
     Lipoprost
     ONO 1608
CN
CN
     Palux
CN
     PGE1
     Prostaglandin E1
CN
CN
     Prostandin
     Prostandin 500
CN
     SEPA-alprostadil
CN
     SEPA-PGE1
CN
     SEPA-prostaglandin El
CN
CN
     Topiglan
CN
     U 10136
FS
     STEREOSEARCH
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MF
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CI
     COM
                  ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
LC
     STN Files:
       BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT,
       CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL,
       DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
       MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH,
       PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
         (*File contains numerically searchable property data)
                      EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

Absolute stereochemistry. Double bond geometry as shown.

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8388 REFERENCES IN FILE CA (1962 TO DATE)

140 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

8393 REFERENCES IN FILE CAPLUS (1962 TO DATE)

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:336101

2: 137:333176 REFERENCE

137:320617 REFERENCE 3:

REFERENCE 4: 137:289308

137:284137 REFERENCE 5:

137:276102 REFERENCE 6:

REFERENCE 7: 137:268473

137:268468 REFERENCE 8:

REFERENCE 9: 137:268402

REFERENCE 10: 137:261859

L171 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2002 ACS

RN 745-64-2 REGISTRY

Prosta-5,13,17-trien-1-oic acid, 9,11,15-trihydroxy-, ÇN (5Z, 9.alpha., 11.alpha., 13E, 15S, 17Z) - (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-1,5octadienyl)cyclopentyl]-, stereoisomer (8CI)

OTHER NAMES:

CN PGF3.alpha.

CN Prostaglandin F3.alpha.

FS STEREOSEARCH

DR 27954-06-9

MF C20 H32 O5

CI COM

STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, LC IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPATFULL (\*File contains numerically searchable property data)

Absolute stereochemistry. Double bond geometry as shown.

```
HO (CH<sub>2</sub>) 3 CO<sub>2</sub>H

Z
Et

R
R
R
E
S
OH
```

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

```
53 REFERENCES IN FILE CA (1962 TO DATE)
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4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

53 REFERENCES IN FILE CAPLUS (1962 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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1: 137:333176
REFERENCE
                136:145563
REFERENCE
            2:
REFERENCE
            3:
                135:231699
REFERENCE
                135:133281
                135:730
REFERENCE
            5:
REFERENCE
            6:
                133:271683
REFERENCE
            7:
                133:161954
REFERENCE
            8:
                132:217154
REFERENCE
            9:
                131:139614
REFERENCE
          10:
                130:343052
L171 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2002 ACS
     745-62-0 REGISTRY
RN
CN
     Prost-13-en-1-oic acid, 9,11,15-trihydroxy-, (9.alpha.,11.alpha.,13E,15S)-
     (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Cyclopentaneheptanoic acid, 3,5-dihydroxy-2-(3-hydroxy-1-octenyl)- (8CI)
CN
     Prostaglandin F1 (7CI)
OTHER NAMES:
CN
     9.alpha.,11.alpha.,15(S)-Trihydroxy-13-trans-prostenoic acid
CN
     PGF1.alpha.
     Prostaglandin F1.alpha.
CN
CN
     U 18714
     STEREOSEARCH
FS
DR
     21562-44-7
     C20 H36 O5
MF
CI
     COM
                  AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
     STN Files:
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU,
       EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NAPRALERT,
```

Absolute stereochemistry.

NIOSHTIC, RTECS\*, TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)

Double bond geometry as shown.

```
HO (CH_2)_6 CO_2H E S (CH_2)_4 Me
```

CN

CN

CN

Enzaprost F

PGF2.alpha.

Panacelan

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

```
927 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
927 REFERENCES IN FILE CAPLUS (1962 TO DATE)
26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
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REFERENCE 1: 137:336040 REFERENCE 2: 137:333176 137:198587 REFERENCE 3: REFERENCE 137:91724 4: REFERENCE 5: 137:68169 137:62644 REFERENCE 6: REFERENCE 7: 136:406871 REFERENCE 8: 136:384140 9: 136:367424 REFERENCE REFERENCE 10: 136:350707 L171 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2002 ACS 551-11-1 REGISTRY RN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, CN (5Z, 9.alpha., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-(8CI) OTHER NAMES: CN(+)-Prostaglandin F2.alpha. CN 7-[3,5-Dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-5-heptenoic acid 9.alpha., 11.alpha., 15(S)-Trihydroxy-5-cis-13-trans-prostadienoic acid CN CN 9.alpha., 11.alpha.-PGF2 CN Amoglandin CN Cyclosin CN Cyclosin (pharmaceutical) CN Dinoprost CN Enzaprost

```
CN
     Prostaglandin F2
CN
     Prostaglandin F2.alpha.
     Prostarmon F
CN
CN
     Prostin F 2 alpha
CN
     Protamodin
CN
     U 14583
     STEREOSEARCH
FS
     13535-33-6, 99437-94-2
DR
MF
     C20 H34 O5
CI
     COM
LC
     STN Files:
                  ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT,
       IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
         (*File contains numerically searchable property data)
     Other Sources:
```

Absolute stereochemistry. Double bond geometry as shown.

HO 
$$\frac{Z}{CH_2}$$
  $\frac{CH_2}{3}$   $\frac{Z}{CO_2H}$  HO  $\frac{Z}{CO_2H}$   $\frac{CH_2}{4}$   $\frac{A}{Me}$ 

# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

12980 REFERENCES IN FILE CA (1962 TO DATE)
145 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
12988 REFERENCES IN FILE CAPLUS (1962 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
REFERENCE
            1: 137:333482
REFERENCE
            2:
                137:333442
REFERENCE
            3:
                137:320613
REFERENCE
                137:320430
REFERENCE
            5:
                137:316113
REFERENCE
            6:
                137:308502
REFERENCE
            7:
                137:291927
REFERENCE
            8:
                137:289311
REFERENCE
                137:289310
            9:
REFERENCE
          10:
                137:289304
L171 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2002 ACS
RN
     363-24-6 REGISTRY
CN
     Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
```

```
(5Z,11.alpha.,13E,15S) - (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN
     5-Heptenoic acid, 7-[3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxocyclopentyl]-
CN
     5-Heptenoic acid, 7-[3.alpha.-hydroxy-2-(3-hydroxy-1-octenyl)-5-
     oxocyclopentyl] - (7CI)
OTHER NAMES:
     (-)-Prostaglandin E2
CN
     (15S) - Prostaglandin E2
CN
     11.alpha., 15.alpha.-Dihydroxy-9-ketoprosta-5, 13-dienoic acid
CN
     11.alpha., 15.alpha.-Dihydroxy-9-oxo-5-cis, 13-trans-prostadienoic acid
CN
CN
     Cervidil
CN
     Dinoprostone
CN
     1-PGE2
CN
     1-Prostaglandin E2
CN
     Minprostin E2
CN
     PGE2
CN
     Prepidil
CN
     Prostaglandin E2 ,
CN
     Prostenon
CN
     Prostenone
ĊN
     Prostin
CN
     Prostin (prostaglandin)
CN
     Prostin E2
CN
     U 12062
CN
     U 42842
FS
     STEREOSEARCH
MF
     C20 H32 O5
CI
     COM
                  ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
     STN Files:
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB,
       IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC,
       PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2,
       USPATFULL, VETU
         (*File contains numerically searchable property data)
                      EINECS**, WHO
     Other Sources:
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

Absolute stereochemistry. Double bond geometry as shown.

$$CO_2H$$

R

R

E
S
 $CO_2H$ 

Me

HO

OH

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

22848 REFERENCES IN FILE CA (1962 TO DATE)
114 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22886 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:342115

REFERENCE 2: 137:336737

REFERENCE 3: 137:336735

REFERENCE 4: 137:336693

REFERENCE 5: 137:336674

REFERENCE 6: 137:336610

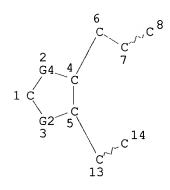
REFERENCE 7: 137:336374

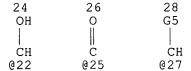
REFERENCE 8: 137:336086

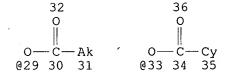
REFERENCE 9: 137:336084

REFERENCE 10: 137:336040

=> d sta que 162 L52 STR







VAR G2=CH2/27
VAR G4=22/25
VAR G5=ME/ET/OH/OME/29/33
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 8
CONNECT IS M1 RC AT 14
CONNECT IS M1 RC AT 35
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

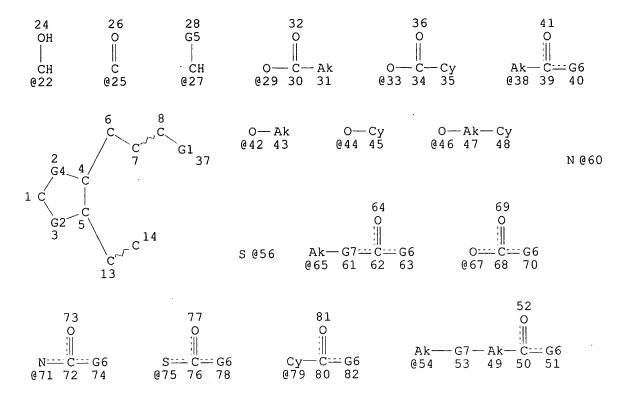
RSPEC 4

NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE

L55 15252 SEA FILE=REGISTRY CSS FUL L52

L61 STR



VAR G1=38/65/54/67/71/75/79

VAR G2=CH2/27

VAR G4=22/25

VAR G5=ME/ET/OH/OME/29/33

VAR G6=OH/42/44/46

VAR G7=0/60/56/CY

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 14

CONNECT IS M1 RC AT 56

CONNECT IS M1 RC AT. 60

CONNECT IS M1 RC AT 71

CONNECT IS M1 RC AT 75

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 4

NUMBER OF NODES IS 65

STEREO ATTRIBUTES: NONE

L62 9692 SEA FILE=REGISTRY SUB=L55 CSS FUL L61

100.0% PROCESSED 15252 ITERATIONS

9692 ANSWERS

SEARCH TIME: 00.00.03

# => d his

(FILE 'HOME' ENTERED AT 13:10:06 ON 04 DEC 2002) SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:10:27 ON 04 DEC 2002 E STJERNSCHANTZ J/AU

```
83 S E3-E7
L1
                E RESUL B/AU
             50 S E3, E4
L2
                E LAKE S/AU
L3
             28 S E3-E7,E11
                E WO98-SE1368/AP, PRN
              1 S E3,E4
L4
                E SE97-2706/AP, PRN
L5
              1 S E4
              1 S L1-L3 AND L4, L5
L6
                SEL RN
     FILE 'REGISTRY' ENTERED AT 13:12:29 ON 04 DEC 2002
             38 S E1-E38
L7
^{R}
             13 S L7 AND 46.150.18/RID AND F/ELS
              5 S L8 AND C5/ES
L9
L10
              2 S L9 NOT SI/ELS
L11
              8 S L8 NOT L9
              3 S L11 AND 3/NR
L12
L13
              1 S L12 NOT SI/ELS
             25 S L7 NOT L8-L13
L14
             9 S L14 AND C5/ES
L15
              6 S L15 NOT SI/ELS
L16
              2 S L16 AND 1/NR
L17
             1 S L17 NOT 4510-16-1
L18
L19
             28 S L7 NOT SI/ELS
L20
             24 S L19 AND NR>=1
             11 S L20 AND (C7H12O2 OR C9H16O OR C7H6BRF OR C11H18O OR C9H19N OR
L21
L22
             13 S L20 NOT L21
     FILE 'REGISTRY' ENTERED AT 13:21:17 ON 04 DEC 2002
     FILE 'HCAPLUS' ENTERED AT 13:22:51 ON 04 DEC 2002
              8 S (PGE2 OR PGE 2 OR PROSTA?) (L) TRIMETHYLENE
L23
              1 S L23 (L) "E2"
L24
              7 S L23 NOT L24
L25
              3 S TRIMETHYLENEPROSTAGLAN?
L26
     FILE 'REGISTRY' ENTERED AT 13:26:02 ON 04 DEC 2002
              1 S 63357-23-3
L27
L28
              1 S 62446-43-9
     FILE 'HCAPLUS' ENTERED AT 13:35:01 ON 04 DEC 2002
          23468 S PGE2 OR PGE 2
L29
           1902 S PG(L)"E2"
L30
L31
          14085 S PROSTAGLANDIN?(L)"E2"
L32
          28658 S L29-L31
            121 S L32 (L) TRINOR
L33
L34
             18 S L33 (L) 18 19 20
             18 S L34 (L) PHENYL
L35
             0 S L34 (L) FLUOROPHENYL
L36
             18 S L34 (L) PHENYL (L) 17
L37
L38
              6 S L37 (L) DIHYDRO
L39
              6 S L38 (L) 13 14
     FILE 'REGISTRY' ENTERED AT 13:40:55 ON 04 DEC 2002
L40
              2 S 55122-62-8 OR 363-24-6
     FILE 'HCAPLUS' ENTERED AT 13:44:17 ON 04 DEC 2002
                SET SMARTSELECT ON
            SEL L39 1- RN :
L41
                                  23 TERMS
```

SET SMARTSELECT OFF

```
FILE 'REGISTRY' ENTERED AT 13:44:18 ON 04 DEC 2002
             23 S L41
L42
             21 S L42 NOT L40
L43
             15 S L43 AND C5/ES
L44
              3 S L44 AND 46.150.18/RID
L45
                E PHXA/CN
              1 S E6
L46
                E PROSTAGLANDIN E/CN
              4 S E3, E19, E20, E47
L47
              1 S E102
L48
              5 S L47, L48
L49
                E PROSTAGLANDIN F/CN
              2 S E12, E25
L50
             5 S E15, E22, E26, E59, E65
L51
L52
                STR
L53
             50 S L52 CSS
                STR L52
L54
L55
          15252 S L52 CSS FUL
                SAV TEMP L55 FAY445/A
                STR L54
L56
             50 S L56 CSS SAM SUB=L55
L57
L58
           9612 S L56 CSS FUL SUB=L55
                SAV TEMP L58 FAY445A/A
L59
                STR L54
              0 S L59 CSS SAM SUB=L58
L60
L61
                STR L56
L62
           9692 S L61 CSS FUL SUB=L55
                SAV TEMP L62 FAY445B/A
L63
              1 S L59 CSS SAM SUB=L62
L64
              1 S L59 SAM SUB=L62
             39 S L59 FUL SUB=L62
L65
                SAV L65 FAY445C/A
           3501 S L55 AND 46.150.18/RID
L66
            558 S L66 AND F/ELS
L67
            236 S L67 AND 1/F
L68
L69
            214 S L68 AND 2/NR
L70
            182 S L69 NOT (SI OR P OR N OR S)/ELS
L71
            11 S L70 AND 3 FLUOROPHENYL
L72
             48 S L55 AND TRINOR
              2 S L72 AND (PGE2 OR "E2")
L73
              3 S L71 AND (C26H37F05 OR C23H33F05 OR C23H31F05)
L74
L75
                STR
              0 S L75 CSS SAM SUB=L55
L76
L77
              4 S L75 CSS FUL SUB=L55
              SAV L77 FAY445D/A
L78
              2 S L77 NOT C23H25F05
L79
              1 S L44 AND C23H38O5
L80
              O S L44 AND TRIMETHYLENE
L81
              1 S L55 AND TRIMETHYLENE
L82
                STR L75
L83
             22 S L82 CSS SAM SUB=L55
L84
            434 S L82 CSS FUL SUB=L55
                SAV FAY4453/A L84
L85
                STR L82
L86
                STR L85
            993 S L86 CSS FUL SUB=L55
L87
                SAV L87 FAY445E/A
L88
              2 S L42 AND L87
             49 S L87 AND C4/ES
L89
L90
             27 S L89 AND 2/NR
L91
                STR L86
L92
            783 S L91 CSS FUL SUB=L87
                SAV L92 FAY445F/A
```

```
L93
             23 S L92 AND C4/ES AND 2/NR
                SEL RN 3-7
             18 S L93 NOT E1-E5
L94
             20 S L78, L94
L95
L96
             8 S L7 AND L55
             24 S L95, L96
L97
              4 S L96 NOT L95
L98
              2 S L98 NOT (4510-16-1 OR 38315-43-4)
L99
             22 S L95, L99
L100
     FILE 'HCAPLUS' ENTERED AT 15:53:47 ON 04 DEC 2002
L101
             11 S L100
L102
             11 S L101 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L103
              4 S L102 AND (?GLAUCOM? OR ?OCULAR? OR ?HYPERTENS? OR EYE)
L104
              3 S L103 AND ?GLAUCOM?
                E GLAUCOMA/CT
                E E4+ALL
           2852 S E5, E4+NT
L105
           4484 S E6, E7, E8, E9/BI
L106
                E E10+ALL
L107
            937 S E3
                E GLAUCOMA/CT
                E E3+ALL
            146 S E15
L108
            178 S E20, E21
L109
              3 S L102 AND L105-L109
L110
L111
              3 S L104, L110
L112
              2 S L1-L6 AND L102
              3 S L111,L112
L113
              8 S L102 NOT L113
L114
L115
              3 S L114 AND TRIMETHYLENE?
                SEL RN L113
     FILE 'REGISTRY' ENTERED AT 15:59:44 ON 04 DEC 2002
L116
             69 S E1-E69
             21 S L55 AND L116
L117
L118
             16 S L100 NOT L117
             15 S L117 NOT L100
L119
     FILE 'HCAPLUS' ENTERED AT 16:01:26 ON 04 DEC 2002
L120
          39837 S L62
L121
          33885 S L120 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L122
            177 S L121 AND L105-L109
L123
            170 S L121 AND ?GLAUCOM?
L124
             97 S L121 AND ?OCULAR? (L) ?HYPERTEN?
L125
            196 S L122, L123, L124
L126
            104 S L125 AND P/DT
L127
             96 S L126 AND (US/PC OR US/PRC OR US/AC)
             88 S L127 AND (PD<=19970711 OR PRD<=19970711 OR AD<=19970711)
L128
L129
             83 S L128 AND ?GLAUCOM?
L130
              5 S L128 NOT L129
              4 S L130 AND ?HYPOTENS?
L131
              1 S L130 NOT L131
L132
L133
             88 S L128-L132
                SEL HIT RN
     FILE 'REGISTRY' ENTERED AT 16:05:40 ON 04 DEC 2002
L134
            506 S E70-E575
             26 S L134 AND NC>=2
L135
              0 S L134 AND IDS/CI
L136
L137
             18 S L134 AND (MXS OR PMS)/CI
L138
             25 S L134 AND (COMPD OR WITH OR UNSPECIFIED)
L139
            480 S L134 NOT L135-L138
```

FILE 'REGISTRY' ENTERED AT 16:09:01 ON 04 DEC 2002

. . .

```
FILE 'HCAPLUS' ENTERED AT 16:09:14 ON 04 DEC 2002
     FILE 'REGISTRY' ENTERED AT 16:09:17 ON 04 DEC 2002
     FILE 'HCAPLUS' ENTERED AT 16:09:31 ON 04 DEC 2002
             3 S L117 AND L113
L140
          37416 S L139
L141
            702 S L141 AND US/PC AND (PD<=19970711 OR PRD<=19970711 OR AD<=1997
L142
            74 S L142 AND L105-L109
L143
L144
             80 S L142 AND (?GLAUCOM? OR ?OCULAR?(L)(?HYPERTENS? OR ?HYPOTENS?
L145
             80 S L143, L144
     FILE 'HCAPLUS' ENTERED AT 16:13:21 ON 04 DEC 2002
            79 S L145 NOT L115, L140
L146
             58 S L146 AND (GLAUCOM? OR OCULAR OR HYPERTENS? OR HYPOTENS? OR IN
L147
             21 S L146 NOT L147
L148
                E PROSTANOID RECEPTOR/CT
L149
            183 S E7
               E E4+ALL
           1203 S E5, E6, E10, E27
L150
           310 S PROSTANOID(L) RECEPTOR(L) EP1
L151
L152
            10 S L149-L151 AND L125
L153
             2 S L145 AND EP1
             10 S L152, L153
L154
             9 S L154 NOT L115, L140
L155
                SEL HIT RN
     FILE 'REGISTRY' ENTERED AT 16:21:47 ON 04 DEC 2002
      64 S E1-E64
L156
L157
             62 S L156 NOT SI/ELS
     FILE 'HCAPLUS' ENTERED AT 16:23:04 ON 04 DEC 2002
L158 .
         29845 S L157
L159
            806 S L158 AND L149-L151
L160
            275 S L159 AND EP1
L161
            132 S L160 AND (PD<=19970711 OR PRD<=19970711 OR AD<=19970711)
             2 S L161 AND L105-L109
L162
             21 S L161 AND (?GLAUCOM? OR ?OCULAR? OR EYE)
L163
L164
             9 S L161 AND (?HYPOTENS? OR ?HYPERTENS? OR PRESSURE)
             9 S L162,L164
L165
             14 S L163 NOT L165
L166
             5 S L155 NOT L165
L167
L168
             4 S L167 NOT DP/TI
L169
             13 S L165, L168
     FILE 'REGISTRY' ENTERED AT 16:29:54 ON 04 DEC 2002
L170
        10 S L49,L50,L51
L171
             9 S L170 AND C5/ES
```

RN 55582-75-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-17-phenyl-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

L169 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:786104 HCAPLUS

DN 123:189195

TI Molecular characterization and ocular hypotensive properties of the prostanoid EP2 receptor

AU Woodward, D. F.; Bogardus, A. M.; Donello, J. E.; Fairbairn, C. E.; Gil, D. W.; Kedzie, K. M.; Burke, J. A.; Kharlamb, A.; Runde, E.; et al.

CS Dep. of Biosciences and Medicinal Chemistry, Allergan Inc., Irvine, CA, USA

SO Journal of Ocular Pharmacology and Therapeutics (1995), 11(3), 447-54
CODEN: JOPTFU; ISSN: 1080-7683

PB Liebert

DT Journal

LA English

CC 2-9 (Mammalian Hormones)

The cloning of the genes that encode for prostaglandin (PG) receptors has AΒ resolved much of the complexity and controversy in this area by confirming the classification proposed by R.A. Coleman; et al. (1994). Two issues that remained unresolved were (1) the inability of the EP2 agonist butaprost to interact with the cloned putative EP2 receptor and (2) mol. biol. confirmations of a 4th PGF2-sensitive receptor, which was pharmacol. designated EP4. To provide clarification, the authors attempted to clone further PGE2-sensitive receptors. By using a cDNA probe that encodes for the human EP3A receptor, a cDNA clone that encoded for a novel PGE2-sensitive receptor was obtained by screening a human placenta library. This cDNA clone was transfected into COS-7 cells for pharmacol. studies. The cDNA clone obtained from human placenta had only .apprx.30% amino acid identity with cDNAs for other PG receptors, including those that encode for the previously proposed murine and human EP2 receptors. Radioligand binding studies on the novel EP receptor expressed in COS-7 cells revealed that selective EP2 agonists such as butaprost, AH 13205, AY 23626 and 19(R)-OH PGE2 all competed with 3H-PGE2 for its binding sites, whereas selective agonists for other PG receptor subtypes had minimal or no effect. This receptor was coupled to adenylate cyclase and EP2 agonists caused dose-related increased in cAMP. It appears that the cDNA described herein encodes for the pharmacol. defined EP2 receptor. Ocular studies revealed that AH 13205 decreased

intraocular pressure in normal and ocular

hypertensive monkeys by a mechanism that does not appear to be involve inhibition of aq. humor secretion.

ST eye ocular pressure prostaglandin EP2 receptor; AH 13205 ocular pressure ITEye

(mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

ΙT Prostaglandin receptors

> RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(EP2, mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

ΙT Receptors

> RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(prostaglandin EP2, mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

IT 60-92-4, CAMP

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

ΙT **363-24-6**, PGE2 148436-63-9, AH 13205

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

TT 9012-42-4, Adenylate cyclase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

TΤ **363-24-6**, PGE2

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mol. characterization and ocular hypotensive properties of the prostanoid EP2 receptor)

363-24-6 HCAPLUS RN

Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, CN (5Z, 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)

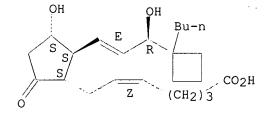
Absolute stereochemistry. Double bond geometry as shown.

```
L115 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
     1980:792 HCAPLUS
ΑN
     92:792
DN
     Prostaglandin E antagonist activity of 11-deoxy-16,16-
TI
     trimethyleneprostaglandin El
     Birnbaum, J. E.; Tolman, E. L.
ΑU
     Biol. Res. Dep., Am. Cyanamid Co., Pearl River, NY, 10965, USA
CS
     Prostaglandins (1979), 18(3), 349-57
SO
     CODEN: PRGLBA; ISSN: 0090-6980
DT
     Journal
     English
LΑ
CC
     2-3 (Hormone Pharmacology)
GI
      (CH2) 6CO2H
           ÓН
                           Ι
     dl-11-Deoxy-16,16-trimethyleneprostaglandin E1 (I) [63357-23-3]
AΒ
     was a potent inhibitor of prostaglandin E-induced contractions of the
     gerbil colon. The antagonism was directed specifically against the
     prostaglandin E receptor and was not manifested when contractions were
     induced by either PGF2.alpha. or acetylcholine.
     prostaglandin E antagonist intestine; deoxytrimethyleneprostaglandin E1
ST
     PGE inhibitor
     Prostaglandins
TΤ
     RL: BIOL (Biological study)
        (E, inhibitor of, deoxytrimethyleneprostaglandin El as, in intestine)
TΤ
     Intestine
        (colon, contraction of, deoxytrimethyleneprostaglandin E1 effect on)
     Molecular structure-biological activity relationship
TΤ
        (prostaglandin E-inhibiting, of trimethylene prostaglandins)
                  62446-41-7 62446-43-9
                                           63295-71-6
                                                        63295-77-2
IΤ
     62407-92-5
     63295-79-4
                  63295-81-8
                               63357-23-3
                                             63357-24-4 63357-25-5
                  63357-28-8
                               63357-30-2
                                             63357-32-4
                                                          63357-34-6
     63357-26-6
     63357-36-8
                  71953-84-9
                               71953-85-0
                                             71953-86-1
                                                          72002-66-5
     72002-67-6
                  72002-68-7
     RL: BIOL (Biological study)
        (as prostaglandin E antagonist, in intestine)
ΙT
     62446-43-9 63357-25-5 63357-26-6
     RL: BIOL (Biological study)
        (as prostaglandin E antagonist, in intestine)
RN
     62446-43-9 HCAPLUS
     5-Heptenoic acid, 7-[2-[3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-
CN
     hydroxy-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3R*),3.alpha.]- (9CI)
     (CA INDEX NAME)
```

Relative stereochemistry.
Double bond geometry as shown.

```
(prepn. and iodination of)
IT
     40899-61-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and isomerization of)
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and oxidn. of)
IT
     62407-83-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and reaction with lithium acetylide)
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and redn. of)
IT
     62407-84-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and trimethylsilylation of)
     63502-09-0P
IT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of)
     542-69-8
IT
    RL: RCT (Reactant)
        (reaction of, with butyllithium and acylobutane carboxylate)
TT
     14924-53-9
     RL: RCT (Reactant)
        (reaction of, with butyllithium and iodobutane)
ΙT
     62446-42-8P 62446-43-9P 63357-25-5P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and bronchodilator activity of)
     62446-42-8 HCAPLUS
RN
     5-Heptenoic acid, 7-[2-[3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-
     hydroxy-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3S*),3.alpha.]- (9CI)
     (CA INDEX NAME)
```

Relative stereochemistry.
Double bond geometry as shown.



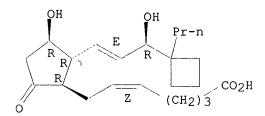
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RN 62446-43-9 HCAPLUS
CN 5-Heptenoic acid, 7-[2-[3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3R*),3.alpha.]- (9CI) (CA INDEX NAME)
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Relative stereochemistry.
Double bond geometry as shown.

RN 63357-25-5 HCAPLUS

CN 5-Heptenoic acid, 7-[3-hydroxy-2-[3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.]-(9CI) (CA INDEX NAME)

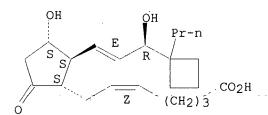
Relative stereochemistry.
Double bond geometry as shown.



RN 63357-26-6 HCAPLUS

CN 5-Heptenoic acid, 7-[3-hydroxy-2-[3-hydroxy-3-(1-propylcyclobutyl)-1-propenyl]-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.]-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L115 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS AN 1977:155256 HCAPLUS

DN 86:155256

TI 16,16-Spirocycloalkylprostaglandins

IN Schaub, Robert E.; Weiss, Martin J.

PA American Cyanamid Co., USA

SO Ger. Offen., 250 pp.

CODEN: GWXXBX

DT Patent

LA German

IC C07C177-00

CC 24-4 (Alicyclic Compounds)

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

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                        Α
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PRAI US 1975-592494
                                        <--
GΙ
```

Ι

II

ΙT

```
Title prostaglandins (e.g., I and II) were prepd. by modifications of
AB
     conventional syntheses, using building blocks for the side chains such as
     1-butylcyclobutanecarboxylic acid (via ethynylation of the corresponding
     aldehyde) and 2-(2-chloroethyl)cyclopropanecarboxylic acid.
     spiroalkyleneprostaglandin; bronchodilator spiroalkyleneprostaglandin;
ST
     gastric juice spiroalkyleneprostaglandin; prostaglandin spiroalkylene
ΙT
     Bronchodilators
        (prostaglandin 16,16-trimethylene derivs.)
ΙT
     Gastric juice
        (secretion of, inhibition of by prostaglandin 16,16-
        trimethylene derivs.)
ΙT
     Prostaglandins
        (derivs., 2,3-methano and 16,16-trimethylene)
     542-69-8
IT
     RL: RCT (Reactant)
        (alkylation of ethyl cyclobutanecarboxylate with)
ΙT
     14924-53-9
     RL: RCT (Reactant)
        (alkylation of, with butyl iodide)
ΙT
     75-24-1
     RL: RCT (Reactant)
        (metalation with, in prostaglandin synthesis)
     41301-95-5
TΤ
     RL: RCT (Reactant)
        (oxidn. of)
     20039-37-6
IT
     RL: RCT (Reactant)
        (oxidn. of 2-(5-hydroxy-1-pentyl)-2-cyclopenten-1-one N-methyl oxime
        with)
     62407-83-4P
TT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and ethynylation of)
     62407-82-3P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and hydride redn. of)
ΙT
     62407-95-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and hydrolysis of)
     62407-85-6P
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and iodination of)
     20434-34-8P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and oxidn. of)
ΙT
     62407-94-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and partial hydrogenation of)
IT
     62443-81-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and partial hydrolysis of)
IT
     62407-86-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and partial redn. of)
     62408-17-7P
TΨ
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and reaction with sodium iodide)
     62408-18-8P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and reaction with triphenylphosphine)
     62408-16-6P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and sapon. of)
     62407-84-5P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and silylation of)
                   62379-24-2P
                                  62387-61-5P
                                                62407-88-9P
                                                               62407-90-3P
IΤ
     62379-23-1P
     62407-99-2P
                    62408-19-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and use in prostaglandin synthesis)
                                              62407-87-8P
     58148-69-9P 58148-71-3P
                                58148-74-6P
IT
                   62407-91-4P
                                  62407-92-5P
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                                                               62407-96-9P
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                                  62446-40-6P
                                                62446-41-7P 62446-42-8P
                    62446-44-0P
     62446-43-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of)
ΙT
     60934-42-1P
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     62408-27-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of, as prostaglandin intermediate)
ΙT
     623-51-8
     RL: RCT (Reactant)
        (reaction of, with 2-[5-[(methylsulfonyl)oxy]pentyl]-2-cyclopenten-1-
        one N-methyl oxime)
     1972-28-7
ΙT
     RL: RCT (Reactant)
        (reaction of, with copper and 4-chloro-1-butene)
ΙT
     927-73-1
     RL: RCT (Reactant)
        (reaction of, with copper and ethyl diazoacetate)
ΙT
     41138-61-8
     RL: RCT (Reactant)
        (reaction of, with dihydropyran)
```

IT 52477-93-7

RL: RCT (Reactant)

(reaction of, with ethyl 2-mercaptoacetate)

IT 1099-45-2 5367-24-8 19093-51-7 21591-31-1 40098-44-0 49826-07-5

RL: RCT (Reactant)

(use of, in prostaglandin synthesis)

IT 58148-71-3P 62446-42-8P 62446-43-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

RN 58148-71-3 HCAPLUS

CN 5-Heptenoic acid, 7-[2-[3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3hydroxy-5-oxocyclopentyl]-, [1R-[1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.]](9CI) (CA INDEX NAME)

Absolute stereochemistry.

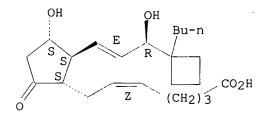
Double bond geometry as shown.

RN 62446-42-8 HCAPLUS

CN 5-Heptenoic acid, 7-[2-[3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.



RN 62446-43-9 HCAPLUS

CN 5-Heptenoic acid, 7-[2-[3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, [1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

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=>
=>
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### => d all hitstr tot 1169

L169 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:770134 HCAPLUS

DN 137:279023

TI Preparation of thromboxane ligands without blood clotting side effects

IN Burk, Robert M.; Krauss, Achim H. P.; Woodward, David F.

PA Allergan, Inc., USA

SO U.S., 18 pp., Cont.-in-part of U.S. Ser. No. 331,356, abandoned. CODEN: USXXAM

DT Patent

LA English

IC ICM C07D307-93 ICS A01K031-343

NCL 514469000

CC 26-3 (Biomolecules and Their Synthetic Analogs) Section cross-reference(s): 1, 63

FAN.CNT 6

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
ΡĪ	US 6462077 US 5416106 US 5516791 US 5650431	B1 A A A	20021008 19950516 19960514 19970722		US 2001-899713 US 1993-174534 US 1995-378414 US 1996-645467	20010705 < 19931228 < 19950126 < 19960513 <
	US 5741812	Α	19980421		US 1997-832431	19970402 <
PRAI	US 1993-174534 US 1995-378414	A3 A2	19931228 19950126	<		
	US 1996-645467	A2	19960513	<		•
	US 1997-832431	A1	19970402	<		
	US 1998-38068 US 1999-331356	B1 B2	19980311 19990616			
OS GI	MARPAT 137:27902		19990010			

$$\begin{array}{c|c}
A - X \\
\hline
O & Z \\
\hline
I
\end{array}$$

AB Thromboxane agonists of formula I [A = alkylene, alkenylene, etc.; B = Me, cycloalkyl, aryl, heteroaryl, etc.; X = (substituted) CH2OH, (substituted) CO2H, etc.; Y = (CH2)n; n = 1-2; Z = (CH2)m; m = 0-1] are prepd. The compds. are used for the treatment of ocular hypotension, hypertension, hemorrhage, myocardial ischemia, angina pectoris, coronary contraction, cerebrovascular contraction after subarachnoidal hemorrhage, cerebral hemorrhage and asthma. Thus, II was prepd. from U-46619 in two steps. II exhibited pronounced activity in contracting vascular smooth muscle.

ΙI

- ST thromboxane ligand prepn ocular hypotension; hemorrhage treatment thromboxane agonist prepn
- Thromboxanes
  RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
  (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses) (agonists; prepn. of thromboxane ligands without blood clotting side effects) Heart, disease IT (angina pectoris; prepn. of thromboxane ligands without blood clotting side effects) ΙT Thromboxanes RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (antagonists; prepn. of thromboxane ligands without blood clotting side effects) IT Brain, disease (hemorrhage; prepn. of thromboxane ligands without blood clotting side effects) ΙT Heart, disease (ischemia; prepn. of thromboxane ligands without blood clotting side effects) IT Hypotension (ocular; prepn. of thromboxane ligands without blood clotting side effects) ΙT Cell aggregation (platelet; prepn. of thromboxane ligands without blood clotting side ITAsthma Cardiac contraction Hemorrhage Human Hypertension (prepn. of thromboxane ligands without blood clotting side effects) IT Thromboxane receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (prepn. of thromboxane ligands without blood clotting side effects) Hypertension ΙT (pulmonary; prepn. of thromboxane ligands without blood clotting side effects) ΙT Meninges (subarachnoid hemorrhage; prepn. of thromboxane ligands without blood clotting side effects) Prostanoid receptors ΙT RL: BSU (Biological study, unclassified); BIOL (Biological study) (type EP; prepn. of thromboxane ligands without blood clotting side effects) ΙT Prostanoid receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (type EP1; prepn. of thromboxane ligands without blood clotting side effects) ΙT Prostanoid receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (type EP3; prepn. of thromboxane ligands without blood clotting side effects) 167270-44-2P ΙT RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of thromboxane ligands without blood clotting side effects) 159359-97-4P 159359-98-5P 159359-94-1P 159359-95-2P IΤ 167270-49-7P 193149-59-6P 193149-60-9P 193149-61-0P 193149-62-1P 167270-51-1P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(prepn. of thromboxane ligands without blood clotting side effects) T5-31-0, Isopropylamine, reactions 551-11-1, PGF2.alpha.

(Uses)

3282-30-2, Trimethylacetyl chloride 56985-40-1, U-46619 RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of thromboxane ligands without blood clotting side effects) 65147-38-8P 71845-64-2P 135877-48-4P IT 136198-86-2P 147555-69-9P 147555-72-4P 159359-93-0P 167270-42-0P 167270-43-1P 167270-45-3P 167270-46-4P 159359-96-3P 167270-48-6P 304854-64-6P 167270-47-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of thromboxane ligands without blood clotting side effects) RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) Anon; EP 0364417 1990 HCAPLUS (2) Bito; US 4599353 A 1986 HCAPLUS (3) Bito, L; Applied Pharmacology in the Medical Treatment of Glaucomas 1984, P477 HCAPLUS (4) Bito, L; Arch Ophthalmol 1987, V105, P1036 MEDLINE (5) Burk; US 5416106 A 1995 HCAPLUS (6) Burk; US 5516791 A 1996 HCAPLUS (7) Burk; US 5741812 A 1998 HCAPLUS (8) Burk; Tetrahedron Letters 1993, V34(3), P395 HCAPLUS (9) Chan; US 4994274 A 1991 HCAPLUS (10) Chan; US 5034413 A 1991 HCAPLUS (11) Coleman, R; Br J Pharmacol V73, P773 HCAPLUS (12) Grover; US 4931460 A 1990 HCAPLUS (13) Larock; US 4436934 A 1984 HCAPLUS (14) Lieb; US 4622339 A 1986 HCAPLUS (15) Nilsson; Invest Ophtalmol Vis Sci 1987, suppl, P284 (16) Siebold; Prodrug 1989, V5, P3 (17) Starr, M; Exp Eye Research 1971, P170 HCAPLUS IT **551-11-1**, PGF2.alpha. RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of thromboxane ligands without blood clotting side effects) 551-11-1 HCAPLUS RN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, CN

(5Z, 9.alpha., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO  $\begin{array}{c} \text{CO}_{2}\text{HO} \\ \text{R} \\ \text{R} \\ \text{R} \end{array}$   $\begin{array}{c} \text{CO}_{2}\text{H} \\ \text{CH}_{2}\text{)}_{4} \\ \text{Me} \\ \text{OH} \end{array}$ 

Absolute stereochemistry.
Double bond geometry as shown.

HO 
$$\frac{Z}{(CH_2)_3}$$
 O Ph

RN 135877-48-4 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, phenylmethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 136198-86-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, methyl ester, (52,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

L169 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:344852 HCAPLUS

DN 131:5147

TI Preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl

```
derivatives for use as ocular hypertensive agents
IN
     Burk, Robert M.
PA
     Allergan Sales, Inc., USA
SO
     PCT Int. Appl., 49 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K031-557
     ICS C07D277-30
CC
     26-3 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1, 63
FAN.CNT 3
     PATENT NO.
                      KIND
                            DATE
                                            APPLICATION NO.
                                                             DATE
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PΙ
     WO 9925358
                       A1
                            19990527
                                            WO 1998-US24481 19981117
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             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR,
                     GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA,
                     GN, GW, ML, MR, NE, SN, TD, TG
                                            US 1997-974067
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                                            CA 1998-2310630
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     AU 9914616
                       A1
                            19990607
                                            AU 1999-14616
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                       A1
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                                            EP 1998-958612
                                                             19981117
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             IE, FI
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                                            NO 2000-2217
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PRAI US 1997-974067
                       Α
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                       А3
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     US 1996-740883
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     US 1997-861414
                       A2
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                                       <--
     WO 1998-US24481
                       W
                            19981117
OS
     MARPAT 131:5147
GΙ
R10
                      R
R10
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AB F-type prostaglandins I [R = heteroaryl such as thienyl; R1 = H, alkyl; X = OH, alkyloxy; Y = :O, H2] were prepd. and formulated for use as ocular hypertensive agents. Thus, thienylprostaglandin II was prepd.

st

IΤ

TΤ

IΤ

IΤ

IT

IΤ

IT

IT

225661-55-2P

```
starting from [4-(2,5-dichloro-3-thienyl)-2-oxobutyl]-phosphonic acid
di-Me ester and (3a.alpha.,4.alpha.,5.beta.,6a.alpha.)-hexahydro-2-oxo-5-
[(tetrahydro-2H-pyran-2-yl)oxy]-2H-cyclopenta[b]furan-4-carboxaldehyde.
The prepd. compds. were tested for binding activity to various
prostanoid receptors, including EP1, EP2, and
EP3.
prostaglandin ocular hypertensive prepn; prostanoid receptor
binding prostaglandin prepn
Prostanoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
   (EP2; prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl
   derivs. for use as ocular hypertensive agents)
Prostanoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
   (EP3; prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl
   derivs. for use as ocular hypertensive agents)
Prostaglandins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
   (F-type; prepn. of cyclopentane heptan(ene)oic acid,
   2-heteroarylalkenyl derivs. for use as ocular hypertensive
   agents)
Prostanoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
   (prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl
   derivs. for use as ocular hypertensive agents)
225660-96-8P 225660-97-9P 225660-98-0P
225660-99-1P 225661-00-7P 225661-65-4P
225661-66-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
   (prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl
   derivs. for use as ocular hypertensive agents)
                                             225661-03-0P
185067-61-2P
               225661-01-8P
                              225661-02-9P
                                             225661-07-4P
                                                            225661-08-5P
                              225661-06-3P
               225661-05-2P
225661-04-1P
225661-09-6P 225661-10-9P 225661-11-0P
225661-12-1P 225661-13-2P 225661-14-3P
               225661-16-5P 225661-17-6P
                                           225661-19-8P
225661-15-4P
225661-22-3P 225661-24-5P 225661-27-8P
225661-30-3P 225661-32-5P 225661-34-7P
                            225661-41-6P
                                           225661-43-8P
225661-36-9P 225661-39-2P
225661-44-9P 225661-46-1P 225661-48-3P
                                        225661-54-1P
225661-50-7P 225661-51-8P 225661-52-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
   (prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl
   derivs. for use as ocular hypertensive agents)
                                 75-30-9, 2-Iodopropane
                                                          141 - 43 - 5,
75-04-7, Ethylamine, reactions
                                              143393-77-5
                                                            185067-71-4
                                 17814-85-6
2-Hydroxyethylamine, reactions
185068-04-6
              225661-67-6
                            225661-69-8
                                         225661-70-1
                                                       225661-71-2
225661-75-6 225661-77-8 225661-79-0
              225661-83-6 225661-84-7
225661-82-5
RL: RCT (Reactant); RACT (Reactant or reagent)
   (prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl
   derivs. for use as ocular hypertensive agents)
```

225661-56-3P **225661-57-4P** 

225661-59-6P

225661-60-9P 225661-61-0P 225661-62-1P 225661-63-2P

225661-64-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as ocular hypertensive agents)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Allergan Inc; WO 9636599 A 1996 HCAPLUS
- (2) Allergan Inc; WO 9731895 A 1997 HCAPLUS
- (3) Burk, R; US 5834498 A 1998 HCAPLUS
- IT 225660-96-8P 225660-97-9P 225660-98-0P 225660-99-1P 225661-00-7P 225661-65-4P 225661-66-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as ocular **hypertensive** agents)

RN 225660-96-8 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-cyano-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 225660-97-9 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-[(1E, 3S)-3-hydroxy-5-(3,4,5-trichloro-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

HO<sub>2</sub>C 
$$(CH_2)$$
  $\frac{1}{3}$   $\frac{1}{2}$   $\frac{1}{2}$ 

RN 225660-98-0 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4,5-dichloro-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

HO<sub>2</sub>C 
$$(CH_2)$$
  $\frac{1}{3}$   $\frac{1}{2}$   $OH$   $E$   $S$   $R$   $R$   $OH$   $C1$ 

RN 225660-99-1 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(5-iodo-3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

$$HO_2C$$
 (CH<sub>2</sub>)  $3$   $Z$  OH  $E$   $S$   $R$  OH  $R$   $R$  OH  $R$ 

RN 225661-00-7 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-2-[(1E, 3S)-5-(4-bromo-2, 5-dimethyl-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME).

Relative stereochemistry. Double bond geometry as shown.

$$HO_2C$$
  $(CH_2)_3$   $Z$   $OH$   $Br$   $Me$   $S$   $R$   $R$   $OH$   $Me$ 

RN 225661-65-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(3R)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxypentyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

HO<sub>2</sub>C 
$$(CH2)3$$
  $Z$   $OH$   $R$   $S$   $R$   $R$   $OH$   $Br$ 

RN 225661-66-5 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(2,5-dibromo-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 185067-61-2P 225661-10-9P 225661-11-0P 225661-12-1P 225661-13-2P 225661-14-3P

225661-15-4P 225661-17-6P 225661-22-3P

225661-24-5P 225661-27-8P 225661-30-3P

225661-32-5P 225661-34-7P 225661-39-2P

225661-44-9P 225661-46-1P 225661-48-3P

225661-51-8P 225661-52-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl

derivs. for use as ocular hypertensive agents)

RN 185067-61-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(2,5-dichloro-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

$$HO_2C$$
 $(CH_2)_3$ 
 $Z$ 
 $HO$ 
 $S$ 
 $R$ 
 $R$ 
 $OH$ 
 $C1$ 
 $S$ 
 $R$ 
 $R$ 
 $R$ 
 $R$ 
 $C1$ 

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-cyano-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

$$i-Pro$$
 $(CH_2)_3$ 
 $Z$ 
 $OH$ 
 $E$ 
 $S$ 
 $R$ 
 $OH$ 
 $OH$ 

RN 225661-11-0 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3,4,5-trichloro-2-thienyl)-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

RN 225661-12-1 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

i-Pro (CH<sub>2</sub>)
$$\frac{1}{3}$$
 $\frac{1}{2}$ OH

Br

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(2,5-dibromo-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

RN 225661-14-3 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

$$(CH_2)_3$$
  $Z$   $OH$   $E$   $S$   $R$   $Me$   $OH$   $Br$   $Br$ 

RN 225661-15-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-chloro-5-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

HO<sub>2</sub>C. 
$$(CH_2)_3$$
 Z OMe  $E$  S Me  $R$  OH  $R$ 

RN 225661-17-6 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-chloro-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

HO<sub>2</sub>C. (CH<sub>2</sub>) 
$$\stackrel{\circ}{_{3}}$$
  $\stackrel{\circ}{_{2}}$   $\stackrel{\circ}{_{2}}$  OH  $\stackrel{\circ}{_{2}}$   $\stackrel{\circ}{_{3}}$   $\stackrel{\circ}{_{2}}$   $\stackrel{\circ}{_{3}}$   $\stackrel{\circ}{_{3}}$ 

RN 225661-22-3 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-methoxy-5-(3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 225661-24-5 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-[(1E, 3S)-3-hydroxy-5-(3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

$$HO_2C$$
  $(CH_2)_3$   $Z$   $OH$   $E$   $S$   $R$   $OH$   $Me$ 

RN 225661-27-8 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5R)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

RN 225661-30-3 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

HO<sub>2</sub>C 
$$(CH_2)$$
  $3$   $Z$   $OH$   $E$   $S$   $R$   $R$   $OH$   $Br$   $Br$   $Br$ 

RN 225661-32-5 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-bromo-4-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

$$OMe$$

HO  $OMe$ 
 $OMe$ 

RN 225661-34-7 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(5-iodo-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

$$HO_2C$$
 $(CH_2)_3$ 
 $Z$ 
 $HO$ 
 $S$ 
 $R$ 
 $R$ 
 $OH$ 
 $OH$ 

RN 225661-39-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

$$HO_2C$$
 (CH<sub>2</sub>)  $\frac{1}{3}$   $\frac{1}{2}$  OMe  $\frac{1}{2}$   $\frac{1}$ 

RN 225661-44-9 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

$$OMe$$
 $OMe$ 
 $OMe$ 

RN 225661-46-1 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

RN 225661-48-3 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,5-dibromo-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 225661-51-8 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-2-[(1E, 3S)-5-(3, 5-dibromo-2-thienyl)-3-hydroxy-1-pentenyl]-3, 5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

$$HO_2C$$
 $(CH_2)_3$ 
 $Z$ 
 $OH$ 
 $E$ 
 $S$ 
 $R$ 
 $OH$ 
 $Br$ 

RN 225661-52-9 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-5-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

IT 225661-75-6 225661-77-8 225661-79-0

225661-82-5 225661-84-7
RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl

derivs. for use as ocular hypertensive agents)

RN 225661-75-6 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4,5-dichloro-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

MeO (CH2)
$$3$$
 $Z$ 
OH
ESSRR
OH
C1

RN 225661-77-8 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(5-iodo-3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, methyl ester, (5Z)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

MeO (CH<sub>2</sub>)
$$_3$$
 $_{\overline{Z}}$ OH

HO  $_{\overline{S}}$   $_{\overline{R}}$   $_{\overline{R}}$   $_{\overline{S}}$   $_{\overline$ 

RN 225661-79-0 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

MeO (CH<sub>2</sub>)
$$\frac{Z}{Z}$$
HO S R E S Me

RN 225661-82-5 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-2-[(3R)-5-(2,5-dibromo-3-thienyl)-3-hydroxypentyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

MeO (CH<sub>2</sub>)
$$\frac{1}{3}$$
 $\frac{1}{2}$  HO S R R S OH Br

RN 225661-84-7 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3,4,5-trichloro-2-thienyl)-1-pentenyl]cyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

MeO (CH<sub>2</sub>) 
$$\frac{Z}{Z}$$
 OH  $\frac{E}{S}$  C1 OH C1

## IT 225661-57-4P 225661-64-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl

derivs. for use as ocular hypertensive agents)

RN 225661-57-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-cyano-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

MeO (CH<sub>2</sub>)
$$\frac{1}{3}$$
 $\frac{1}{2}$  OH OH

RN 225661-64-3 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(3R)-5-(2,5-dichloro-3-thienyl)-3-hydroxypentyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

MeO (CH<sub>2</sub>)
$$_3$$
 $_{\overline{Z}}$ OH Cl

L169 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:720997 HCAPLUS

DN 128:10580

TI Key role cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow of the newborn

AU Li, Ding-You; Hardy, Pierre; Abran, Daniel; Martinez-Bermudez, Ana-Katherine; Guerguerian, Anne-Marie; Bhattacharya, Mousumi; Almazan, Guillermina; Menezes, Ravi; Peri, Krishna G.; Varma, Daya R.; Chemtob, Sylvain

CS Dep. Pharmacol. Therapeutics, McGill Univ., Montreal, H3G 1Y6, Can.

SO American Journal of Physiology (1997), 273(4, Pt. 2), R1283-R1290 CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal

LA English

CC 2-9 (Mammalian Hormones)

AB Ibuprofen, a cyclooxygenase (COX) inhibitor nonselective for either COX-1 or COX-2 isoform, upregulates cerebrovascular prostaglandin E2 (PGE2) and

PGF2.alpha. receptors in newborn pigs. COX-2 was shown to be the predominant form of COX and the main catalyst of prostaglandin synthesis in the newborn brain. We proceeded to establish direct evidence that COX-2-generated prostaglandins govern PGE2 and PGF2.alpha. receptor d. and function in the cerebral brain vasculature by using newborn. Hence, we detd. PGE2 and PGF2.alpha. receptor d. and functions in brain vasculature by using newborn pigs treated with saline, ibuprofen, COX-1 inhibitor (valerylsalicylate), or COX-2 inhibitors (DUP-697 and NS-398). Newborn brain PGE2 and PGF2.alpha. concns. were significantly reduced by ibuprofen, DUP-697, and NS-398 but not by valerylsalicylate. In newborn pigs treated with DUP-697, NS-398, and ibuprofen, PGE2 and PGF2.alpha. receptor densities in brain microvessels were increased to adult levels; there was also a significant increase in inositol 1,4,5-trisphosphate (IP3) prodn. and cerebral vasoconstrictor effects of 17-phenyltrinor-PGE2 (EP1 receptor agonist), M&B-28767 (EP3 receptor agonist), PGF2.alpha., and fenprostalene (PGF2.alpha. analog). Treatment with ibuprofen or DUP-697 also increased the upper blood pressure limit of cerebral cortex and periventricular blood flow autoregulation from 85 to .gtoreg.125 mmHg (uppermost blood pressure studied). However, valerylsalicylate treatment did not affect cerebrovascular PGF2 and PGF2.alpha. receptors, IP3 prodn., or vasoconstrictor effects in newborn animals. These in vivo and in vitro observations indicate that COX-2 is mainly responsible for the regulation of PGE2 and PGF2.alpha. receptors and their functions in the newborn cerebral vasculature. cyclooxygenase prostaglandin receptor brain circulation newborn; PGF2 receptor brain circulation newborn cyclooxygenase; PGE2 receptor brain circulation newborn cyclooxygenase

IT Prostanoid receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(EP1; cyclooxygenase-2 in PGE2 and PGF2.alpha.

receptor regulation and cerebral blood flow in newborn pigs)

IT Prostanoid receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(EP3; cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT Prostanoid receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(FP; cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT Circulation

(cerebral; cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT Brain

ST

Newborn

Vasoconstriction

(cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT Blood vessel

(microvessel; cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT 39391-18-9

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(2; cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT 363-24-6, PGE2 551-11-1, PGF2.alpha. 38315-43-4,

17-Phenyltrinor-PGE2 **60972-43-2**, M&B-28767 69381-94-8, Fenprostalene

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT 88269-39-0, Inositol 1,4,5-trisphosphate

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

IT 363-24-6, PGE2 551-11-1, PGF2.alpha. 60972-43-2 , M&B-28767

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(cyclooxygenase-2 in PGE2 and PGF2.alpha. receptor regulation and cerebral blood flow in newborn pigs)

RN 363-24-6 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

$$\frac{Z}{R}$$
  $\frac{Z}{R}$   $\frac{CO_2R}{R}$   $\frac{E}{HO}$   $\frac{CO_2R}{N}$   $\frac{CO_2R}{N}$ 

RN 551-11-1 HCAPLUS CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

HO 
$$\frac{Z}{CO_2H}$$
  $\frac{CH_2)_4}{HO}$   $\frac{Z}{CO_2H}$ 

RN 60972-43-2 HCAPLUS

CN Cyclopentaneheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]-5-oxo-, (1S,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

L169 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:272439 HCAPLUS

DN 126:339206

TI Prostaglandin effects on the contractility of bovine trabecular meshwork and ciliary muscle

AU Krauss, Achim H.-P.; Wiederholt, Michael; Strum, Annette; Woodward, David F.

CS Allergan, Inc., Irvine, CA, 92612, USA

SO Experimental Eye Research (1997), 64(3), 447-453

CODEN: EXERA6; ISSN: 0014-4835

PB Academic

DT Journal

LA English

AB

CC 2-9 (Mammalian Hormones)

The ocular hypotensive activity of prostaglandins (PGs) has previously been demonstrated in various species including man. underlying mechanism of action of prostanoids other than PGF2.alpha. remains contentious. Because the trabecular meshwork and ciliary muscle are believed to have a role in the regulation of aq. humor outflow, the aim of this study was to identify the PG-receptor subtypes present in these tissues using receptor-selective agonists. Contractions of isolated strips of bovine trabecular meshwork and ciliary muscle were recorded isometrically in continuously perfused tissue chambers. Contractile activity of PGs was detd. relative to a maximally effective concn. of carbachol (1 .mu.M) as a std. agonist. following prostanoids were employed: PGF2.alpha., 17-Ph PGF2.alpha. (FP-receptor agonists), sulprostone (EP3 > EP1-agonist), AH13205 (EP2-agonist), 11-deoxy PGE1 (non-selective EP-agonist), and U-46619 (TP-agonist). The thromboxane-mimetic U-46619 elicited a strong contraction of the trabecular meshwork with the highest concn. (1 .mu.M) being almost twice as efficacious (186.6%) as the maximal carbachol concn., whereas the effect on the ciliary muscle was small. The U-46619 induced trabecular meshwork contraction could be blocked with a potent and selective TP-receptor antagonist, 1 .mu.M SQ29548, indicating the involvement of TP-receptors. The other PG-analogs studied had either no or a small but statistically significant Thus, 17-Ph PGF2.alpha. (1 .mu.M) weakly contracted the ciliary muscle (4.8%), sulprostone (1 .mu.M) the trabecular meshwork (10.1%). 11-Deoxy PGE1 (1 .mu.M) and AH13205 (10 .mu.m) elicited relaxations in both tissues precontracted with carbachol (1 .mu.M). The relaxant effects were more pronounced in trabecular meshwork (15.6% for 11-deoxy PGE1 and PGF2.alpha. 21.4% for AH13205) than ciliary muscle (6.8 and 7.4% resp.). did not elicit a significant response in either tissue. The studies suggest the existence of TP- and EP2-receptors in the bovine trabecular meshwork and potentially FP- and EP2-receptors in the ciliary muscle. In conclusion, thromboxane-mimetics and EP2-agonists have opposing activities on contractile elements in the meshwork and may modulate trabecular outflow in a functionally antagonistic manner. Prostanoid effects on ciliary muscle appear rather modest compared to parasympathomimetic drugs. It is conceivable that TP-agonists may

substantially affect trabecular outflow.

ST prostaglandin eye ciliary muscle trabecular meshwork; PGF 2alpha eye

IT Eye

Eye

(ciliary muscle; prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Muscle

Muscle

(ciliary; prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Prostaglandins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Thromboxane receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Eye

(trabecular meshwork; prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT 551-11-1, PGF2.alpha. 37786-00-8, 11-Deoxy PGE1

**55582-75-7**, 17-Phenyl PGF2.alpha. 56985-40-1, U-46619

60325-46-4, Sulprostone 148436-63-9, AH13205

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT **551-11-1**, PGF2.alpha. **37786-00-8**, 11-Deoxy PGE1

**55582-75-7**, 17-Phenyl PGF2.alpha.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

RN 551-11-1 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO 
$$\frac{Z}{R}$$
  $\frac{CH_2)_3}{R}$   $\frac{CO_2H}{Me}$ 

RN 37786-00-8 HCAPLUS

CN Prost-13-en-1-oic acid, 15-hydroxy-9-oxo-, (13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

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L169 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ΑN
     1995:621888 HCAPLUS
DN
     123:169428
     7-[Carboxyalkyl or alkenyl]-6-[alkyl or alkenyl]-3-oxo-2,4-
ΤI
     dioxabicyclo[3.2.1]octanes and their derivatives
     Burk, Robert M.; Krauss, Achim H.; Woodward, David F.
ΙN
PΑ
     Allergan, Inc., USA
SO
     U.S., 10 pp.
     CODEN: USXXAM
DT
     Patent
LA
     English
IC
     ICM A61K031-335
     ICS C07D493-08
NCL
     514450000
     26-3 (Biomolecules and Their Synthetic Analogs)
CC
     Section cross-reference(s): 2
FAN.CNT 6
     PATENT NO.
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                             DATE
                                            APPLICATION NO.
                                                              DATE
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                                            US 1993-174534
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             RU, SD, SE, SK, UA, UZ, VN
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
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                     CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
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                       Т3
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     US 1998-38068
                       В1
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                             19990616
     US 1999-331356
OS
     MARPAT 123:169428
GΙ
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Ι

Dioxabicyclooctanes I [R = (un)substituted CO2H, CH2OH, CH2NH2; R1 = OH, AΒ acyloxy, O] were prepd. for use in treating ocular hypertension. Thus, PGF2.alpha. was esterified, silylated, treated with triphosgene, subjected to borohydride redn., and deblocked to qive I [R = CH2OH, R1 = OH]. At 0.1% this compd. decreased intraocular pressure in dogs by 8.5mm 6 h after administration. ST thromboxane analog dioxabicyclooctane; ocular hypertension dioxabicyclooctane; prostaglandin receptor dioxabicyclooctane; platelet aggregation inhibitor dioxabicyclooctane IT Blood platelet aggregation inhibitors Glaucoma (disease) (analogs; dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) ITThromboxanes RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (analogs; dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) ITProstaglandin receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) ITReceptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (prostaglandin, dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) IT167270-47-5P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) ΙT 159359-94-1P 159359-95-2P 159359-97-4P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) IT **551-11-1**, PGF2.alpha. RL: RCT (Reactant); RACT (Reactant or reagent) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) 33854-16-9P, PGF2.alpha. methyl ester 65147-38-8P 71845-64-2P 135877-48-4P 136198-86-2P 159359-93**-**0P 147555-69-9P **147555-72-4P** 159359-96-3P 167270-45-3P 167270-46-4P 167270-48-6P 167270-42-0P 167270-43-1P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) 167270-49-7P 167270-50-0P 167270-51-1P TT 159359-98-5P 167270-44-2P RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) 551-11-1, PGF2.alpha. TΤ RL: RCT (Reactant); RACT (Reactant or reagent) (dioxabicyclooctane analogs of thromboxanes in treatment of ocular hypertension) RN 551-11-1 HCAPLUS

Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,

CN

(5Z, 9.alpha., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO 
$$\frac{Z}{CH_2}$$
  $\frac{CH_2}{3}$   $\frac{Z}{CO_2H}$  HO  $\frac{Z}{CO_2H}$   $\frac{CH_2}{4}$   $\frac{A}{Me}$ 

IT 33854-16-9P, PGF2.alpha. methyl ester 65147-38-8P
71845-64-2P 135877-48-4P 136198-86-2P
147555-72-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(dioxabicyclooctane analogs of thromboxanes in treatment of

ocular hypertension)

RN 33854-16-9 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, methyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 65147-38-8 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11-dihydroxy-, methyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 71845-64-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, phenylmethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO
$$\begin{array}{c} \text{CH}_2)_3 \\ \text{R} \\ \text{R} \\ \text{R} \\ \text{E} \\ \text{S} \\ \text{OH} \\ \text{O} \\ \text{Me} \\ \end{array}$$

RN 135877-48-4 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, phenylmethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 136198-86-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, methyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 147555-72-4 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11-dihydroxy-, phenylmethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

L169 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:215124 HCAPLUS

DN 122:232

TI Pharmacological characterization of prostaglandin-related ocular hypotensive agents

AU Goh, Yasumasa; Kishino, Junji

CS Shionogi Research Laboratories, Toyonaka, 561, Japan

SO Japanese Journal of Ophthalmology (1994), 38(3), 236-45 CODEN: JJOPA7; ISSN: 0021-5155

PB Japanese Journal of Ophthalmology

DT Journal

LA English

CC 1-2 (Pharmacology)

AB The agonistic activity of the prostaglandin (PG)-related ocular hypotensive agents, S-1033, UF-021 and PhXA34, to PG receptors was investigated by using in vitro tissue responses and binding of radio-labeled ligands to membranes. UF-021 and PhXA34, which are both 1-iso-Pr esterified forms, were examd. mainly in a free acid form. The agonistic activity to PGD2 and PGI2 receptors, examd. using inhibition of ADP-induced aggregation of guinea pig platelets, was negligible for all three compds. None showed substantial agonistic activity to TXA2 receptor, as detd. from contractions of rat thorax aorta. PhXA34 showed

significant PGE2 agonistic activity. Among the three PGE2 receptor subtypes, the agonistic activity to EP1 and EP2 receptors was about 1/1000 and 1/2000 of PGE2, as detd. from contraction of guinea pig longitudinal and circular ileum strips, resp. The other two compds. showed little agonistic activity (<1/100 000 of PGE2) to these receptors. The agonistic activity to PGF2.alpha. receptors, as detd. from contraction of cat iris sphincter strips, was substantial for S-1033 and PhXA34, being 1/45 and 1/2 of PGF2.alpha., resp., but weak for UF-021 (1/1600). further investigate the affinity of the three compds. to PGE2 and PGF2.alpha. receptors, inhibition of [3H] PGE2.alpha. binding was examd. with membrane fractions of bovine adrenal medulla which possesses EP3 type PGE2 receptors and bovine corpus luteum which has PGF2.alpha. receptors. The activity of PhXA34 for inhibiting [3H]PGE2 binding was about 1/2000 of S-1033 and UF-021 did not significantly inhibit [3H]PGE2 binding within the range examd. (<<1/2000 of PGE2). The activity to inhibit [3H] PGF2.alpha. binding was strong for PhXA34 (about the same as that of PGF2.alpha.), while the activity for S-1033 and UF-021 was about 1/34 and <1/280 of PGF2.alpha., resp. These results indicate that the specificity to PGF2.alpha. receptor is the highest for S-1033 followed by PhXA34 although the activity to this receptor is stronger for the latter compd. UF-021 has only a weak agonistic activity to PGF2.alpha. receptors. S1033 UF021 PhXA34 prostaglandin thromboxane receptor; eye hypotensive S1033 UF021 PhXA34 prostaglandin Prostaglandin receptors Thromboxane receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (ocular hypotensive agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors) Glaucoma (disease) (ocular hypotensive agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors in relation to **glaucoma** treatment) Receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (prostaglandin, ocular hypotensive agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors) Receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (thromboxane, ocular hypotensive agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors) 120373-24-2, UF-021 138282-73-2, S-1033 155551-81-8, PhXA34 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (ocular hypotensive agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors) 120373-24-2, UF-021 138282-73-2, S-1033 **155551-81-8**, PhXA34 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (ocular hypotensive agents S-1033, UF-021, and PhXA34

agonistic activity to prostaglandin and thromboxane receptors)

oxodecyl)cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-(3-

Absolute stereochemistry. Double bond geometry as shown.

120373-24-2 HCAPLUS

ST

ΙT

ΙT

IΤ

TΤ

TT

TΨ

RN

CN

i-Pro (CH<sub>2</sub>)
$$_3$$
 $_{\overline{Z}}$ 
HO  $_{\overline{S}}$   $_{\overline{R}}$   $_{\overline{CH_2}}$   $_{\overline{6}}$   $_{\overline{Me}}$ 

RN 138282-73-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11-dihydroxy-, monosodium salt, (5Z,9.alpha.,11.alpha.,13E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

HO
$$\begin{array}{c} \text{S} & \text{R} \\ \text{R} & \text{R} \end{array}$$

$$\begin{array}{c} \text{CO}_2\text{H} \\ \text{(CH}_2)_5 \end{array}$$

Na

RN 155551-81-8 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenylpentyl)cyclopentyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

OH 
$$CH_2-CH=CH-(CH_2)_3-C-OPr-i$$
 OH  $CH_2-CH_2-CH_2-CH_2-Ph$ 

L169 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:500557 HCAPLUS

DN 121:100557

TI EP3 receptor-mediated inhibition of the neurogenic vasopressor response in pithed rats

AU Malinowska, Barbara; Godlewski, Grzegorz; Buczko, Wlodzimierz; Schlicker, Eberhard

CS Zaklad Famakodynamiki, Akademia Medyczna, ul. Mickiewicza 2C, Bialystok, 15-230/8, Pol.

SO European Journal of Pharmacology (1994), 259(3), 315-19 CODEN: EJPHAZ; ISSN: 0014-2999

DT Journal

LA English

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L140 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
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AN 1999:64692 HCAPLUS

DN 130:119579

 ${\tt TI} \quad {\tt Prostaglandin} \ {\tt derivatives} \ {\tt devoid} \ {\tt of} \ {\tt side} \ {\tt effects} \ {\tt for} \ {\tt the} \ {\tt treatment} \ {\tt of} \ {\tt glaucoma}$ 

PA Pharmacia & Upjohn AB, Swed.

SO PCT Int. Appl., 40 pp. CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-557

CC 1-1 (Pharmacology)

Section cross-reference(s): 26

FAN CNT 1

FAN.CNI I																		
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			LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NΖ,	PL,
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			CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG						
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PRAI SE 1997-2706
                       Α
                            19970711
                                     <--
                            19980710 <--
     WO 1998-SE1368
                       W
     MARPAT 130:119579
os
     A new method and compns. for the treatment of glaucoma and
AB
     ocular hypertension are described. The method is based
     on the usage of EP1 prostanoid receptor agonists which effectively reduce
     the intraocular pressure but have no, or reduced effect on iris
     pigmentation. The prostaglandin analog which is an EP1 selective agonist
     is applied topically on the eye.
ST
     prostaglandin treatment glaucoma
     Prostanoid receptors
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (EP1; prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
IT
     Antiglaucoma agents
       Glaucoma (disease)
        (prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
ΙT
     Prostaglandins
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
TT
     4510-16-1P, Pgf2.beta. 38315-43-4P 219827-59-5P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
     130225-92-2P 157019-93-7P 219827-55-1P
TΤ
                    219827-85-7P 219828-15-6P
     219827-63-1P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
     75-30-9, Isopropyl iodide
                                75-77-4, Trimethylsilyl chloride, reactions
TT
     456-41-7, 3-Fluorobenzyl bromide
                                        688-73-3, Tributyltin hydride
     1195-42-2, N-Isopropylcyclohexylamine
                                             4202-14-6, Dimethyl
                              14924-53-9, Ethyl cyclobutanecarboxylate
     2-oxopropylphosphonate
                  61305-36-0
                              149862-39-5
     31752-99-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
                                             62407-83-4P
                                                             62407-84-5P
                   39990-99-3P
                                 62407-82-3P
ΙT
     38754-71-1P
                                                                219827-87-9P
                   219827-74-4P
                                  219827-77-7P
                                                 219827-83-5P
     63295-65-8P
                                   219827-95-9P
                    219827-93-7P
                                                  219827-98-2P
                                                                 219828-01-0P
     219827-90-4P
                                   219828-09-8P
                                                  219828-13-4P
     219828-04-3P
                    219828-07-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prostaglandin derivs. devoid of side effects for treatment of
        glaucoma)
RE.CNT
              THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alcon Laboratories, Inc; WO 9408585 A1 1994 HCAPLUS
(2) Bays, D; Natural product reports 1990, V7(5), P409 MEDLINE
```

(4) Watabe, A; The Journal of Biological Chemistry 1993, V268(27), P20175

(3) Kluender, H; US 4132738 A 1979 HCAPLUS

**HCAPLUS** 

(5) Woodward, D; Journal of Lipid Mediators 1993, V6, P545 HCAPLUS

IT 4510-16-1P, Pgf2.beta. 38315-43-4P 219827-59-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prostaglandin derivs. devoid of side effects for treatment of glaucoma)

RN 4510-16-1 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 38315-43-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 219827-59-5 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(1E)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, methyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

## IT 130225-92-2P 157019-93-7P 219827-55-1P

219827-63-1P 219828-15-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prostaglandin derivs. devoid of side effects for treatment of glaucoma)

RN 130225-92-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 157019-93-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 219827-55-1 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(1E)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 219827-63-1 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(3R)-5-(3-fluorophenyl)-3-hydroxypentyl]-3-hydroxy-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

OH 
$$\overline{Z}$$
  $(CH_2)_3$   $OPr-i$ 

RN 219828-15-6 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(3R)-5-(3-fluorophenyl)-3-hydroxypentyl]-3-hydroxy-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

OH 
$$\overline{Z}$$
  $(CH_2)_3$   $CO_2H$ 

R
R
R
R
R

L140 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:533851 HCAPLUS

DN 121:133851

TI Preparation of prostaglandin F2.beta. isopropyl ester for the treatment of **glaucoma** 

IN Myazaki, Tooru; Kawamura, Masanori; Shirasawa, Eiichi

PA Ono Pharmaceutical Co, Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp. CODEN: JKXXAF

DT Patent

```
LA
    Japanese
    ICM C07C405-00
IC
    ICS A61K031-557
    26-3 (Biomolecules and Their Synthetic Analogs)
    Section cross-reference(s): 1
FAN.CNT 1
    PATENT NO.
                     KIND
                          DATE
                                         APPLICATION NO.
                                                         DATE
                     ____
                          _____
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    JP 06100529
                     A2
                           19940412
                                         JP 1992-278039
PΙ
                                                        19920922 <--
    CASREACT 121:133851
OS
GΙ
```

AB The title compd. (I) (R = H) (II) was prepd. by hydrolysis of I (R = tetrahydropyran-2-yl) (III). A soln. of III in 5% acetic acid-THF was stirred for 1.5 h at 65.degree. to give II. A 0.02% soln. of II decreased intraocular pressure in rabbits by 5 mmHg.

ST prostaglandin isopropyl ester prepn glaucoma; glaucoma treatment prostaglandin isopropyl ester

IT Glaucoma (disease)

(prostaglandin F2.beta. iso-Pr ester effect on)

T

IT 64-19-7, Acetic acid, uses

RL: USES (Uses)

(hydrolysis of tetrahydropyranyloxyprostaglandin deriv. in water and)

IT 157019-94-8P 157019-95-9P 157019-96-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prepn. of agent for treatment of glaucoma)

IT 157019-93-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, for treatment of glaucoma)

IT 67-63-0, 2-Propanol, reactions 37786-09-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, in prepn. of agent for treatment of glaucoma)

IT 157019-93-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, for treatment of glaucoma)

RN 157019-93-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9.beta.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO 
$$\frac{Z}{(CH_2)_3}$$
 OPr-i  $\frac{Z}{RR}$  OH O  $\frac{Z}{(CH_2)_4}$  Me

```
L140 ANSWER 3 OF 3 HCAPLUS
                             COPYRIGHT 2002 ACS
     1990:605515 HCAPLUS
ΑN
DN
     113:205515
ΤI
     Preparation and use of prostaglandin derivatives for the treatment of
     glaucoma or ocular hypertension
     Stjernschantz, Johan W.; Resul, Bahram
ΙN
PΑ
     Pharmacia AB, Swed.
SO
     PCT Int. Appl., 39 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
IC
     ICM A61K031-557
     ICS
         C07C177-00
CC
     2-9 (Mammalian Hormones)
     Section cross-reference(s): 1, 26
FAN.CNT 1
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                            DATE
                                            APPLICATION NO.
                                                             DATE
     PATENT NO.
                                            _____
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     WO 9002553
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     AT 227576
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                                            US 1994-202409
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Α

US 5578618

19961126

US 1995-390394

19950216 <--

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CC
     2-9 (Mammalian Hormones)
     In pithed rats, the authors studied the effects of prostaglandin E2 and of
AΒ
     subtype-selective prostaglandin E receptor (EP receptor
     ) ligands on the rise in blood pressure induced by elec.
     stimulation of the preganglionic sympathetic nerves. Prostaglandin E2,
     the EP1/EP3 receptor agonist sulprostone and the
     EP2/EP3 receptor agonist misoprostol inhibited the elec. induced
     increase in diastolic blood pressure (rank order of potencies
     sulprostone .gtoreq. misoprostol .gtoreq. prostaglandin E2); the rise in
     blood pressure induced by exogenously added noradrenaline was
     not affected by these compds. The inhibitory effect of sulprostone on the
     elec. induced vasopressor response was not significantly changed by
     indomethacin. Iloprost (an agonist at EP1 and prostacyclin
     receptors (IP receptors)) failed to affect the elec.
     evoked increase in blood pressure. The present study suggests
     that prostaglandin E2 inhibits the release of catecholamines in pithed
     rats via prostanoid receptors of the EP3 subtype,
     probably located presynaptically on the postganglionic sympathetic nerve
ST
     prostaglandin EP3 receptor neurogenic vasopressor response; blood
     pressure sympathetic nerve PGE3 receptor
     Catecholamines
ΙT
     RL: BIOL (Biological study)
        (release of, in neurogenic vasopressor response, PGE3 inhibition of,
        EP3 receptor mediation of)
IT
     Blood pressure
        (sympathetic nerve elec. stimulation increase of, PGE3 inhibition of,
        EP3 receptor mediation of)
ΙT
     Prostaglandin receptors
     RL: BIOL (Biological study)
        (EP3, neurogenic vasopressor response inhibition by PGE3 mediation by)
ΙT
     Receptors
     RL: BIOL (Biological study)
        (prostaglandin EP3, neurogenic vasopressor response
        inhibition by PGE3 mediation by)
ΙT
     Nerve
        (sympathetic, blood pressure increase by elec. stimulation
        of, PGE3 inhibition of, EP3 receptor mediation of)
                                                             60325-46-4,
ΙT
     363-24-6, Prostaglandin E2
                                  59122-46-2, Misoprostol
     Sulprostone
     RL: BIOL (Biological study)
        (neurogenic vasopressor response inhibition by, EP3 receptor mediation
        of)
ΙT
     363-24-6, Prostaglandin E2
     RL: BIOL (Biological study)
        (neurogenic vasopressor response inhibition by, EP3 receptor mediation
        of)
     363-24-6 HCAPLUS
RN
CN
     Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,
     (5Z,11.alpha.,13E,15S) - (9CI) (CA INDEX NAME)
```

Absolute stereochemistry. Double bond geometry as shown.

$$CO_2H$$

R

R

R

CO<sub>2</sub>H

CO<sub>2</sub>H

Me

HO

OH

L169 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:290674 HCAPLUS

DN 120:290674

TI Reduced responses of retinal vessels of the newborn pig to prostaglandins but not to thromboxane

AU Abran, Danile; Varma, Daya R.; Li, Ding-You; Chemtob, Sylvain

CS Dep. Ped., Centre Res. Hopital Sainte-Justine, Montreal, QC, HET 1C5, Can.

SO Canadian Journal of Physiology and Pharmacology (1994), 72(2), 168-73
CODEN: CJPPA3; ISSN: 0008-4212

DT Journal

LA English

AΒ

CC 2-9 (Mammalian Hormones)

The upper blood pressure limit of retinal blood flow autoregulation is lower in the newborn than in the adult; this suggests an insufficient vasoconstrictor response in the newborn when perfusion pressure is increased. Because prostaglandins (PGs) have an important role in autoregulation of retinal blood flow, the authors compared the effects of PGE2, PGF2.alpha., carbacyclin (PGI2 analog), and U46619 (thromboxane analog), as well as that of agonists for the three different PGE2 receptor subtypes, 17-Ph trinor PGE2 (EP1), butaprost (EP2), and M&B 28, 767 (EP3), on the retinal vasculature of newborn and adult pigs, using isolated eyecup prepns. PGF2.alpha. and PGE2 caused a markedly greater constriction of retinal arteries and veins of the adult than of the newborn animals. Further anal. of the response to PGE2, using receptor subtype agonists revealed that the EP1 receptor agonist, 17-Ph trinor PGE2, and the EP3 receptor agonist, M&B 28, 767, caused a significant constriction of adult arteries and veins but produced minimal effects on newborn vessels; the EP2 receptor agonist, butaprost, caused a small and comparable dilation of newborn and adult arteries and veins. The PGI2 analog, carbacyclin caused a greater dilation of the adult than of the newborn arteries, but produced comparable dilation of veins from both newborn and adult animals. contrast to the effects of PGF2.alpha. and PGE2, the thromboxane analog, U46619, as well as the .alpha.1-adrenoceptor agonist, phenylephrine, significantly constricted newborn arteries and veins, and this effect was comparable with that obsd. on retinal vessels of the adult. The authors' findings indicate that the retinal vasculature of the newborn responds minimally to prostaglandins, primarily PGF2.alpha. and PGE2, compared with the adult, but constricts effectively to thromboxane. Since prostaglandins play an important role in the autoregulation of retinal blood flow, the authors' observations provide an explanation for the inability of the newborn to limit blood flow when perfusion pressure is raised.

ST retina vasoconstriction newborn prostaglandin thromboxane

IT Newborn

(eye retina vasoconstriction response to prostaglandins and thromboxanes in)  $\$ 

IT Blood pressure

(eye retina vasoconstriction response to prostaglandins and

thromboxanes in newborn in relation to) IT Prostaglandins Thromboxanes RL: BIOL (Biological study) (eye retina vasoconstriction response to, in newborn) ΙT Circulation (of eye retina, prostaglandins and thromboxanes effect on, in newborn) ΙT Vein (retinal, constriction of, prostaglandins and thromboxanes stimulatory sensitivity of, in newborn) IT Prostaglandins RL: BIOL (Biological study) (EP1 receptors, eye retina vasoconstriction response to PGE2 mediation by, in newborn and adult) ΙT Prostaglandins RL: BIOL (Biological study) (EP3 receptors, eye retina vasoconstriction response to PGE2 mediation by, in newborn and adult) IT Receptors RL: BIOL (Biological study) (prostaglandin EP1, eye retina vasoconstriction response to PGE2 mediation by, in newborn and adult) IT Receptors RL: BIOL (Biological study) (prostaglandin EP3, eye retina vasoconstriction response to PGE2 mediation by, in newborn and adult) IT (retina, vasoconstriction response to prostaglandins and thromboxanes in) IT Artery (retinal, constriction of, prostaglandins and thromboxanes stimulatory sensitivity of, in newborn) IT 59-42-7, Phenylephrine **363-24-6**, PGE2 **551-11-1**, PGF2.alpha. 56985-40-1, U-46619 RL: BIOL (Biological study) (eye retina vasoconstriction response to, in newborn) IT 363-24-6, PGE2 551-11-1, PGF2.alpha. RL: BIOL (Biological study) (eye retina vasoconstriction response to, in newborn)

Absolute stereochemistry.

RN

CN

Double bond geometry as shown.

363-24-6 HCAPLUS

$$\frac{Z}{R}$$
  $\frac{Z}{R}$   $\frac{CO_2H}{R}$   $\frac{E}{HO}$   $\frac{CO_2H}{Me}$ 

551-11-1 HCAPLUS RN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, CN (5Z, 9.alpha., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)

Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11.alpha.,13E,15S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO 
$$\frac{Z}{SR}$$
  $\frac{Z}{RR}$   $\frac{CO_2H}{Me}$   $\frac{CO_2H}{Me}$ 

```
L169 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2002 ACS
     1994:290654 HCAPLUS
DN
     120:290654
ΤI
     Studies on the ocular hypotensive effects of prostaglandin
     F2.alpha. prodrugs and receptor selective prostaglandin analogs
ΑU
     Woodward, David F.; Chan, M. F.; Burke, J. A.; Cheng-Bennett, A.; Chen,
     G.; Fairbairn, C. E.; Gac, T.; Garst, M. E.; Gluchowski, C.; et al.
CS
     Dep. Biochem., Allergan, Inc., Irvine, CA, USA
     Journal of Ocular Pharmacology (1994), 10(1), 177-93
SO
     CODEN: JOPHER; ISSN: 8756-3320
DT
     Journal
     English
LA
CC
     2-9 (Mammalian Hormones)
AΒ
     The use of natural prostaglandins (PG), such as PGD2, PGE2, PGF2.alpha.,
     and PGI2, for treating glaucoma is limited by their ocular side
     effects. One approach to achieve the required sepn. of ocular
     hypotensive activity from side effects is to employ ester
     prodrugs. From a novel series of 11- and 15-mono and 11,15-diacyl esters
     of PGF2.alpha. the authors identified prodrugs where PGF2.alpha. formation
     rates in the iris-ciliary body exceeded those in the conjunctiva, sclera,
     and corneal endothelium. Compared to PGF2.alpha.-1-iso-Pr ester the
     ocular tissue hydrolysis rates of the 11-monopivaloyl, the
     11,15-dipivaloyl ester and the 1,11-lactone were .ltoreq.1000-fold less.
     Despite this large disparity in hydrolysis rates, the pivaloyl esters and
     the 1,11-lactone were potent ocular hypotensives in the authors'
     animal models. In studying prostaglandin analogs, the authors found that
     a diverse variety of prostanoid receptor selective
     agonists lowered intraocular pressure in dogs and/or monkeys.
     These included DP-, EP1-, EP2-, EP3-, and FP-receptor
     -selective compds. The receptor selectivity of these agonists
     was reexamd. by radioligand binding studies. Using radiolabeled PGE2,
     17-Ph PGF2.alpha., and sulprostone the authors were able to confirm the
     selectivity of the agonists currently used for receptor
     characterization directly by radioligand binding competition studies. It
     appears that multiple prostanoid receptor subtypes may
     be involved in regulating intraocular pressure.
     prostanoid receptor subtype intraocular pressure; PGF 2alpha
ST
     prodrug ocular hypotensive
ΙT
     Eye, metabolism
        (conjunctiva, PGF2.alpha. formation from ester prodrugs in)
ΙT
     Eye, metabolism
        (cornea, epithelium, PGF2.alpha. formation from ester prodrugs in)
IT
     Eye, metabolism
        (cornea, stroma, PGF2.alpha. formation from ester prodrugs in)
IT
        (intraocular fluid, PGF2.alpha. prodrugs hypotensive effect
ΙT
     Eye, metabolism
        (iris-ciliary body, PGF2.alpha. formation from ester prodrugs in)
IT
     Uterus, composition
```

(myometrium, prostanoid receptors of, prostanoid ligands interaction with)

IT Receptors

RL: BIOL (Biological study)

(prostaglandin, subtypes, of ocular tissues, intraocular pressure modulation by)

IT Prostaglandins

RL: BIOL (Biological study)

(receptors, subtypes, of ocular tissues, intraocular **pressure** modulation by)

IT **363-24-6**, PGE2 **40666-16-8**, Fluprostenol 41598-07-6,

PGD2 **60972-43-2**, MB 28767 148436-63-9, AH 13205

RL: BIOL (Biological study)

(myometrium prostanoid receptors interaction with)

IT 37786-00-8, 11-Deoxy PGE1 53764-90-2 55314-48-2,

PGF2.alpha. 1,9-lactone 55314-49-3, PGF2.alpha. 1,15-lactone

**55582-75-7**, 17-Phenyl PGF2.alpha. 56985-40-1, U 46619

60325-46-4, Sulprostone 62410-84-8, PGF2.alpha. 1,11-lactone

134217-11-1 135273-39-1 135273-43-7

137143-41-0 154887-01-1 154887-02-2

RL: PRP (Properties)

(ocular hypotensive effect of)

IT **551-11-1**, PGF2.alpha.

RL: BIOL (Biological study)

(prodrug hydrolysis to, in eye, ocular hypotensive effect of)

IT 363-24-6, PGE2 40666-16-8, Fluprostenol

**60972-43-2,** MB 28767

RL: BIOL (Biological study)

(myometrium prostanoid receptors interaction with)

RN 363-24-6 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

$$CO_2H$$

R

R

CO<sub>2</sub>H

CO<sub>2</sub>H

CO<sub>2</sub>H

Me

OH

RN 40666-16-8 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-[3-(trifluoromethyl)phenoxy]-1-butenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 60972-43-2 HCAPLUS

CN Cyclopentaneheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]-5-oxo-, (1S,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

IT 37786-00-8, 11-Deoxy PGE1 53764-90-2 55582-75-7, 17-Phenyl PGF2.alpha. 134217-11-1 135273-39-1

135273-43-7

RL: PRP (Properties)

(ocular hypotensive effect of)

RN 37786-00-8 HCAPLUS

CN Prost-13-en-1-oic acid, 15-hydroxy-9-oxo-, (13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 53764-90-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO
$$\begin{array}{c|c} & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & &$$

RN 55582-75-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-17-phenyl-, (52,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 134217-11-1 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO 
$$\frac{Z}{CH_2}$$
  $\frac{CH_2}{3}$   $CO_2H$   $\frac{E}{HO}$   $\frac{CCH_2}{4}$   $\frac{A}{Me}$   $\frac{Bu-t}{O}$ 

RN 135273-39-1 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-bis(2,2-dimethyl-1-oxopropoxy)-9-hydroxy-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 135273-43-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11-(2,2-dimethyl-1-oxopropoxy)-9,15-dihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HO
$$S R$$

$$R R$$

$$E$$

$$OH$$

$$OH$$

$$OH$$

$$CO_2H$$

$$Me$$

$$OH$$

IT **551-11-1**, PGF2.alpha.

RL: BIOL (Biological study)

(prodrug hydrolysis to, in eye, ocular hypotensive effect of)

RN 551-11-1 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO 
$$\frac{Z}{SR}$$
  $\frac{Z}{RR}$   $\frac{CO_2H}{RR}$   $\frac{E}{RO}$   $\frac{CO_2H}{Me}$   $\frac{CO_2H}{Me}$ 

L169 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:596454 HCAPLUS

DN 119:196454

TI Intraocular **pressure** effects of selective prostanoid receptor agonists involve different receptor subtypes according to radioligand binding studies

AU Woodward, David F.; Lawrence, Ruth A.; Fairbairn, Casey E.; Shan, Tanwir;

Williams, Linda S. CS Dep. Biol. Sci., Allergan, Inc., Irvine, CA, 92713-9534, USA SO Journal of Lipid Mediators (1993), 6(1-3), 545-53 CODEN: JLMEEG; ISSN: 0921-8319 DT Journal LA English 2-9 (Mammalian Hormones) CC The receptors involved in the ocular hypotensive AΒ activity PGE2 and PGF2.alpha. in dogs and monkeys were investigated by examg. the effects of putative receptor selective agonists on intraocular pressure. A diverse variety of receptor selective agonists lowered intraocular pressure in these species. Thus, FP-receptor agonists (17-Ph PGF2.alpha., fluprostenol), agonists with potent activity at the EP3 receptor (MB 28767, sulprostone) and a prostanoid with activity at the EP2 receptor (11-deoxy PGE1) were all potent ocular hypotensives when administered as a single dose to dogs and monkeys or b.i.d. for 5 days in monkeys. These findings were regarded as surprising and prompted re-exam. of some aspects of the current classification for prostanoid receptors. At present certain receptor subtypes, notably EP2, EP3, and FP receptors, are defined only according to potency rank order for agonists. In these studies, the authors employed radioligand binding studies to det. the degree of competition between prostanoid agonists claimed to be selective on the basis of functional assays. Competition studies with the myometrial plasma membrane prepd. from the rat uterus were consistent with the presence of an EP3 receptor. Thus, EP3-receptor agonists (MB 28767 and sulprostone) potently inhibited PGE2 and sulprostone binding, whereas FP agonists (17-Ph PGF2.alpha., fluprostenol), a DP agonist (BW 245C), an EP1 antagonist (AH 6809), and EP2 agonist (AH 13205) and TP-receptor ligands (BM 13505, I-BOP) afforded little or no inhibition. Radioligand binding studies in plasma membrane prepns. from the rat colon with 17-Ph [3H] PGF2.alpha. were consistent with the presence of an FPreceptor. 17-Ph [3H]PGF2.alpha. was potently displaced by PGF2.alpha., whereas only very weak competition at the receptor site was afforded by EP3 agonists (MB 28767, sulprostone). The results are consistent with the existence of EP3 and FP receptors as distinct entities. The findings also imply that the decrease in intraocular pressure produced by FP and EP3 agonists results from stimulation of two independent subpopulations of prostanoid receptors. STeye intraocular pressure prostaglandin receptor agonist ΙT (intraocular pressure of, prostaglandin receptor subtypes in regulation of) ΙT Prostaglandins RL: BIOL (Biological study) (EP3 receptors, in eye intraocular pressure regulation) IT Prostaglandins RL: BIOL (Biological study) (FP receptors, in eye intraocular pressure regulation) ΙT Receptors RL: BIOL (Biological study) (prostaglandin EP3, in eye intraocular pressure regulation) ITReceptors RL: BIOL (Biological study) (prostaglandin FP, in eye intraocular pressure regulation) 37786-00-8, 11-Deoxy PGE1 40666-16-8, Fluprostenol ΙT **55582-75-7**, 17-Phenyl PGF2.alpha. 60325-46-4, Sulprostone 60972-43-2, MB 28767

RL: BIOL (Biological study)

(eye intraocular pressure decrease by)

IT 37786-00-8, 11-Deoxy PGE1 40666-16-8, Fluprostenol
55582-75-7, 17-Phenyl PGF2.alpha. 60972-43-2, MB 28767

RL: BIOL (Biological study)

(eye intraocular pressure decrease by)

RN 37786-00-8 HCAPLUS

CN Prost-13-en-1-oic acid, 15-hydroxy-9-oxo-, (13E,15S)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 40666-16-8 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-[3-(trifluoromethyl)phenoxy]-1-butenyl]cyclopentyl]-, (5Z)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 55582-75-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-17-phenyl-, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 60972-43-2 HCAPLUS

CN Cyclopentaneheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]-5-

oxo-, (1S,2S)-rel- (9CI) (CA INDEX NAME)

```
L169 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2002 ACS
     1993:517000 HCAPLUS
ΑN
DN
     119:117000
     Phenyl-substituted prostaglandins: potent and selective
TТ
     antiglaucoma agents. [Erratum to document cited in
     CA118(11):101683k]
     Resul, Bahram; Stjernschantz, Johan; No, Kiyo; Liljebris, Charlotta;
ΑU
     Selen, Goeran; Astin, Maria; Karlsson, Maritha; Bito, Laszlo Z.
CS
     Kabi Pharm. AB Ophthalmics, Uppsala, Swed.
     Journal of Medicinal Chemistry (1993), 36(15), 2242
SO
     CODEN: JMCMAR; ISSN: 0022-2623
DT
     Journal
     English
LA
CC
     26-3 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1
     3 Errors in the text have been cor. The errors were not reflected in the
AB
     abstr. or the index entries.
ST
     erratum phenyltrinorprostaglandin ester prepn antiglaucoma;
     phenyltrinorprostaglandin ester prepn antiglaucoma erratum;
     glaucoma inhibitor phenyltrinorprostaglandin ester erratum;
     prostaglandin receptor affinity phenyltrinorprostaglandin ester erratum
IT
     Glaucoma (disease)
        (inhibitors, phenyltrinorprostaglandin F esters (Erratum))
IT
     Prostaglandins
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (FP receptors, phenyltrinorprostaglandin F esters affinity for
        (Erratum))
IT
     Receptors
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prostaglandin FP, phenyltrinorprostaglandin F esters
        affinity for (Erratum))
IT
     4202-14-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (benzylation of (Erratum))
IT
     551-11-1 37658-84-7 38344-08-0
     53764-90-2 145667-77-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (intraocular pressure-lowering activity of (Erratum))
ΙT
     31752-99-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (oxidn. of (Erratum))
                    145773-20-2P
TT
     145667-74-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and deacylation of (Erratum))
ΙT
     41639-71-8P 130209-82-4P 130273-87-9P
```

```
145773-22-4P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and intraocular pressure-lowering activity of (Erratum))
     145667-76-1P
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, with carboxybutylphosphonium bromide
        (Erratum))
     41162-19-0P
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, with formyloxabicyclooctanone (Erratum))
     38754-71-1P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, with phenylbutylphosphonate (Erratum))
ΙT
     41639-23-0P
                   41639-72-9P
                                 41639-73-0P 130209-77-7P
                    145773-21-3P
     145667-75-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and redn. of (Erratum))
ΙΤ
     41639-83-2P 41639-84-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn., esterification, and intraocular pressure-lowering activity of
        (Erratum))
ΙT
     130209-76-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn., oxidn., and intraocular pressure-lowering activity of
        (Erratum))
ΙT
     17814-85-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with oxobicyclooctanone deriv. (Erratum))
ΙT
     551-11-1 37658-84-7 38344-08-0
     53764-90-2 145667-77-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (intraocular pressure-lowering activity of (Erratum))
RN
     551-11-1 HCAPLUS
     Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
CN
     (5Z, 9.alpha., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)
Absolute stereochemistry.
Double bond geometry as shown.
```

RN 37658-84-7 HCAPLUS CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15R)- (9CI) (CA INDEX NAME)

HO
$$\begin{array}{c} \text{CO}_{2}\text{H} \\ \text{R} \\ \text{R} \\ \text{R} \end{array}$$

$$\begin{array}{c} \text{CO}_{2}\text{H} \\ \text{CH}_{2}\text{)}_{4} \\ \text{Me} \\ \text{OH} \end{array}$$

RN 38344-08-0 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 53764-90-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 145667-77-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9.alpha.,11.alpha.,13E,15R)- (9CI) (CA INDEX NAME)

HO 
$$\frac{Z}{(CH_2)3}$$
 OPr-i HO  $(CH_2)_4$  Me

# IT 41639-71-8P 130209-82-4P 130273-87-9P 145773-22-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and intraocular pressure-lowering activity of (Erratum))

RN 41639-71-8 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenyl-1-pentenyl)cyclopentyl]-, [1R-[1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 130209-82-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 130273-87-9 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenyl-1-pentenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

RN 145773-22-4 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenylpentyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(S\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

## IT 130209-77-7P

RN 130209-77-7 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E)-3-oxo-5-phenyl-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

#### IT 41639-83-2P 41639-84-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn., esterification, and intraocular pressure-lowering activity of (Erratum))

RN 41639-83-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 41639-84-3 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenylpentyl)cyclopentyl]-, [1R-[1.alpha.(Z),2.beta.(S\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

### IT 130209-76-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn., oxidn., and intraocular pressure-lowering activity of
(Erratum))

RN 130209-76-6 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

L169 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2002 ACS 1993:101683 HCAPLUS ΑN DN 118:101683 Phenyl-substituted prostaglandins: potent and selective TIantiglaucoma agents ΑU Resul, Bahram; Stjernschantz, Johan; No, Kiyo; Liljebris, Charlotta; Selen, Goeran; Astin, Maria; Karlsson, Maritha; Bito, Laszlo Z. CS Kabi Pharm. AB Ophthalmics, Uppsala, Swed. SO Journal of Medicinal Chemistry (1993), 36(2), 243-8 CODEN: JMCMAR; ISSN: 0022-2623 DT Journal LA English

26-3 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1

AB Title compds. I and their 13,14-dihydro derivs. (II) were prepd. and evaluated for their ocular hypotensive effect and side effects in different animal models. In addn., the activity of I and II on FP receptors was studied in vitro. The results were compared with those of PGF2.alpha. and its iso-Pr ester. I and II exhibited good intraocular pressure reducing effect, were more selective, and exhibited a much higher therapeutic index in the eye than PGF2.alpha. or its iso-Pr ester. (15R)-I and II exhibited high activity on FP receptors.

ST phenyltrinorprostaglandin ester prepn antiglaucoma;

ST phenyltrinorprostaglandin ester prepn antiglaucoma; glaucoma inhibitor phenyltrinorprostaglandin ester; prostaglandin receptor affinity phenyltrinorprostaglandin ester

Ι

IT Glaucoma (disease)

(inhibitors, phenyltrinorprostaglandin F esters)

IT Prostaglandins

RL: RCT (Reactant); RACT (Reactant or reagent)

(FP receptors, phenyltrinorprostaglandin F esters affinity for)

IT Receptors

CC

GI

RL: RCT (Reactant); RACT (Reactant or reagent)
 (prostaglandin FP, phenyltrinorprostaglandin F esters
 affinity for)

```
4202-14-6
ΙT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (benzylation of)
     551-11-1 37658-84-7 38344-08-0
TT
     53764-90-2 145667-77-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (intraocular pressure-lowering activity of)
     31752-99-5
TΤ
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (oxidn. of)
ΤТ
     145667-74-9P
                    145773-20-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and deacylation of)
ΙT
     41639-71-8P 130209-82-4P 130273-87-9P
     145773-22-4P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and intraocular pressure-lowering activity of)
ΙT
     145667-76-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, with carboxybutylphosphonium bromide)
ΙT
     41162-19-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, with formyloxabicyclooctanone)
ΙT
     38754-71-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, with phenylbutylphosphonate)
                                 41639-73-0P 130209-77-7P
IT
     41639-23-0P
                   41639-72-9P
     145667-75-0P
                    145773-21-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and redn. of)
IT
     41639-83-2P 41639-84-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn., esterification, and intraocular pressure-lowering activity of)
ΙT
     130209-76-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn., oxidn., and intraocular pressure-lowering activity of)
IΤ
     17814-85-6, 4-Carboxybutyltriphenylphosphonium bromide
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with oxobicyclooctanone deriv.)
     551-11-1 37658-84-7 38344-08-0
IT
     53764-90-2 145667-77-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (intraocular pressure-lowering activity of)
RN
     551-11-1 HCAPLUS
     Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,
CN
     (5Z, 9.alpha., 11.alpha., 13E, 15S) - (9CI) (CA INDEX NAME)
Absolute stereochemistry.
```

HO 
$$\frac{Z}{R}$$
  $\frac{CH_2)_3}{R}$   $\frac{CO_2H}{Me}$  HO OH

RN 37658-84-7 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9.alpha.,11.alpha.,13E,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 38344-08-0 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 53764-90-2 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

```
19981215
     US 5849791
                       Α
                                            US 1995-461334
                                                             19950605 <--
     US 5627208
                       Α
                            19970506
                                            US 1995-470607
                                                             19950606 <--
     JP 08109132
                            19960430
                                            JP 1995-241200
                                                             19950920 <--
                       Α2
     JP 2955213
                       В2
                            19991004
     US 6030999
                            20000229
                                            US 1999-307814
                       Α
                                                             19990510 <--
     US 6187813
                       В1
                            20010213
                                            US 1999-307813
                                                             19990510 <--
     US 6429226
                       В1
                            20020806
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     US 2001-781896
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OS
     MARPAT 113:205515
AB
     Ophthalmol. compns. for topical treatment of glaucoma or
     ocular hypertension comprise, in an ophthalmol.
     compatible carrier, an effective amt. of a deriv. of PGA, PGB, PGD, PGE,
     or PGF having an .omega.-chain C13BC14DR2 [B is a single, double, or
     triple bond between C13 and C14; D = (un)substituted C1-10 chain
     optionally interrupted by O, S, or N; R2 = (un)substituted ring].
     crude 15-(R,S)-17-phenyl-18,19,20-trinor-PGF2.alpha. (prepn. given) was
     esterified and purified by column chromatog. to give 15-(R)-17-phenyl-
     18,19,20-trinor-PGF2.alpha. isopropyl ester (I) in 46% yield. I (10
     .mu.g) reduced intraocular pressure in healthy human volunteers
     to 11.2 mm Hg 8 h after administration (control = 15.1 mm Hg at 8 h).
     and other prepd. prostaglandin derivs. all significantly reduced
     intraocular pressure without significant irritating effect (
     ocular discomfort); 2 of the derivs. caused little, if any,
     conjunctival/episcleral hyperemia in man.
ST
     prostaglandin deriv glaucoma treatment; PGF deriv
     glaucoma treatment
IT
     Glaucoma (disease)
        (treatment of, with prostaglandin derivs.)
IT
     Prostaglandins
     RL: PREP (Preparation)
        (A, 18,19,20-trinor-, 13,14-dihydro-17-Ph, alkyl esters, prepn. of, for
        glaucoma treatment)
ΙT
     Prostaglandins
     RL: PREP (Preparation)
        (A, 18,19,20-trinor-, 15-dehydro-17-Ph, alkyl esters, prepn. of, for
        glaucoma treatment)
ΙT
     Prostaglandins
     RL: PREP (Preparation)
        (E, 18,19,20-trinor-, 13,14-dihydro-17-Ph, alkyl esters, prepn. of, for
        glaucoma treatment)
ΙT
     Prostaglandins
     RL: PREP (Preparation)
        (E, 18,19,20-trinor-, 15-dehydro-17-Ph, alkyl esters, prepn. of, for
        glaucoma treatment)
IT
     Prostaglandins
     RL: PREP (Preparation)
        (F, 18,19,20-trinor-, 13,14-dihydro-17-Ph, alkyl esters, prepn. of, for
        glaucoma treatment)
```

```
ΙT
     Prostaglandins
     RL: PREP (Preparation)
        (F, 18,19,20-trinor-, 15-dehydro-17-Ph, alkyl esters, prepn. of, for
        glaucoma treatment)
     38315-43-4, 17-Phenyl-18,19,20-trinor PGE2 38315-48-9
TT
     38344-08-0 51705-19-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (esterification of, in prepn. of prostaglandin deriv. for
        glaucoma treatment)
ΙT
     38754-71-1P
                   41639-72-9P
                                  52343-56-3P
                                                88257-37-8P
                                                              130209-85-7P
     130273-88-0P
                    130273-89-1P 130273-90-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of, in prostaglandin deriv. prepn. for
        glaucoma treatment)
ΤТ
     130209-75-5P 130209-76-6P 130209-77-7P
                    130209-79-9P 130209-81-3P
     130209-78-8P
     130209-82-4P 130209-83-5P 130209-84-6P
     130225-92-2P 130273-87-9P
     RL: PREP (Preparation)
        (prepn. of, for glaucoma treatment)
                  130209-80-2
TΤ
     31752-99-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, in prepn. of prostaglandin deriv. for glaucoma
        treatment)
     41162-19-0, Dimethyl-2-oxo-4-phenylbutyl phosphonate
TΤ
                                                             52344-42-0
     61263-11-4, Dimethyl-2-oxo-6-phenyl-hexylphosphonate
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, in prostaglandin deriv. prepn. for glaucoma
        treatment)
     75-30-9, Isopropyl iodide
                                 41029-44-1, Isopropyl triflate
IΤ
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with prostaglandin, in prostaglandin deriv. prepn. for
        glaucoma treatment)
     38315-43-4, 17-Phenyl-18,19,20-trinor PGE2 38315-48-9
IT
     38344-08-0 51705-19-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (esterification of, in prepn. of prostaglandin deriv. for
        glaucoma treatment)
     38315-43-4 HCAPLUS
RN
     5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-
CN
     pentenyl]-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)
Absolute stereochemistry.
Double bond geometry as shown.
            ·OH
Ph
         S
                            (CH<sub>2</sub>)3
```

RN 38315-48-9 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

RN 38344-08-0 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-[(1E, 3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 51705-19-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

## IT 130273-90-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prostaglandin deriv. prepn. for **glaucoma** treatment)

RN 130273-90-4 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenyl-1-pentenyl)cyclopentyl]- (9CI) (CA INDEX NAME)

OH
$$CH_{2}-CH = CH - (CH_{2})_{3}-CO_{2}H$$

$$OH$$

$$CH = CH - CH_{2}-CH_{2}-Ph$$

IT 130209-75-5P 130209-76-6P 130209-77-7P 130209-78-8P 130209-81-3P 130209-82-4P 130209-83-5P 130209-84-6P 130225-92-2P

130273-87-9P

RL: PREP (Preparation)
 (prepn. of, for glaucoma treatment)

RN 130209-75-5 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-4-phenyl-1-butenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 130209-76-6 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-[(1E, 3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

RN 130209-77-7 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-[(1E)-3-oxo-5-phenyl-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, <math>(5Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 130209-78-8 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-4-phenoxy-1-butenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 130209-81-3 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-[3-hydroxy-4-(4-methoxyphenyl)-1-butenyl]cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

RN 130209-82-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 130209-83-5 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-6-phenyl-1-hexenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 130209-84-6 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-7-phenyl-1-heptenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3S\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

RN 130225-92-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 130273-87-9 HCAPLUS

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenyl-1-pentenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1.alpha.(Z),2.beta.(1E,3R\*),3.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)



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